

L | E | A | D | E | R  
I T A L I A

# Implants and Biomaterials



Literature review 2011 - 1<sup>st</sup> edition



## Published articles

<b>Scanning electron microscopy (SEM) and X-ray dispersive spectrometry evaluation of direct laser metal sintering surface and human bone interface: a case series</b> Mangano C, Piattelli A, Raspanti M, Mangano F, Cassoni A, Iezzi G, Shibli JA <i>Lasers Medical Science</i> 2011; 26:133–138	5
<b>Early human bone response to laser metal sintering surface topography: a histologic report</b> Mangano C, Piattelli A, D'Avila S, Iezzi G, Mangano F, Onuma T, Shibli JA <i>Journal of Oral Implantology</i> 2010; 36(2):91-96	6
<b>Influence of direct laser fabrication implant topography on type IV bone</b> Shibli JA, Mangano C, D'Avila S, Piattelli A, Pecora GE, Mangano F, Onuma T, Cardoso LA, Ferrari Sanchez D, Aguiar KC, Iezzi G <i>Journal of Biomedical Materials Research Part A</i> 2010; 93:607-614	7
<b>The osteoblastic differentiation of dental pulp stem cells and bone formation on different titanium surface textures</b> Mangano C, De Rosa A, Desiderio V, d'Aquino R, Piattelli A, De Francesco F, Tirino V, Mangano F, Papaccio G <i>Biomaterials</i> 2010; 31:3543-3551	8
<b>A "custom made" implant produced by microfusion of titanium particles: case-report</b> Silvetti M, Mangano C, Macchi A, Mangano F <i>Dental Cadmos</i> 2010, 78(7):133-142	9
<b>Implant surface topography in modern implantology. Part I: smooth and microrough surfaces</b> Mangano F, Mangano C, Macchi A, Perrotti V, Iezzi G, Piattelli A <i>Italian Oral Surgery</i> 2010; 9(4):201-214	10
<b>Implant surface topography in modern implantology. Part II: nanostructured and DLF surfaces</b> Mangano F, Mangano C, Macchi A, Perrotti V, Iezzi G, Piattelli A <i>Italian Oral Surgery</i> 2010; 9(5):261-262, 265-275	11
<b>Immediate loading of modified acid etched dental implants in post-extraction sockets</b> Mangano C, Piattelli A, Mangano F, Perrotti V, Iezzi G <i>Implant Dentistry</i> 2009; 18(2):142-150	12
<b>Dental implants from laser fusion of titanium microparticles: from research to clinical applications</b> Mangano C, Shibli JA, Mangano F, Sammons RL, Macchi A <i>Journal of Osseointegration</i> 2009; 1(1):9-22	13
<b>Stereo imaging and cytocompatibility of a model dental implant surface formed by direct laser fabrication</b> Mangano C, Raspanti M, Traini T, Sammons RL, Piattelli A <i>Journal of Biomedical Materials Research Part A</i> 2009; 88A(3):823-831	14
<b>Two modifications of maxillary sinus lift technique</b> Rapani C, Rapani M <i>Italian Oral Surgery</i> 2009; 8(3):127-134	16
<b>Direct metal laser-sintering per la produzione di impianti "custom made"</b> Macchi A, Taubert Pozzi S, Zecca PA <i>DoctorOS</i> 2009; 8:1086-1087	16
<b>The induction of bone formation by coral-derived calcium carbonate/hydroxyapatite constructs</b> Ripamonti U, Crooks J, Khoali L, Roden L <i>Biomaterials</i> 2009; 30:1428-1439	17
<b>Combining scaffolds and osteogenic cells in regenerative bone surgery</b> Mangano C, Piattelli A, Mangano A, Mangano F, Mangano A, Iezzi G, Borges F, D'Avila S, Shibli JA <i>Clinical Implant Dentistry and Related Research</i> 2009; 11(S1):92-102	18
<b>Early human bone response to laser metal sintering surface topography: a histologic evaluation</b> Shibli JA, Mangano C, Mangano F, Iezzi G, Cardoso L, Onuma T, Ferrari D, Piattelli A. <i>Clinical Oral Implant Research</i> 2009; 20(9):1036	19
<b>Histomorphometric and torque out evaluation of new laser treated implant surfaces: an <i>in vivo</i> study</b> De Benedictis S, Berardi D, Malagola C, Trisi P, Perfetti G <i>Clinical Oral Implant Research</i> 2009; 20(9):1028	20

<i>Scaffolds seeded with stem cells: research and clinical application in bone regeneration</i> Mangano F, Papaccio G, Mangano C <i>Ceramics, cells and tissue 2009; 58 - 12° Annual seminar &amp; Meeting Faenza</i>	
<i>Direct Titanium laser forming implants</i> Macchi A, Mangano C, Mangano F <i>Ceramics, cells and tissue 2009; 59 - 12° Annual seminar &amp; Meeting Faenza</i>	
<i>Valutazione istologica ed ultrastrutturale della risposta ossea intorno ad impianti ottenuti mediante Direct Laser Metal Sintering</i> Esposito P, Mangano C, Raspanti M, Piattelli A, D'Avila S, Pecora G, Mangano F, Iezzi G, Shibli JA <i>Atti XVI° Congresso Collegio Docenti Odontoiatria 2009</i>	
<b>Cellule staminali adulte: una nuova frontiera nella rigenerazione ossea in Odontostomatologia</b> Mangano F, Mangano C, Macchi A, Piattelli A, Montini S <i>Implant Tribune Italian Edition 2008; 1:1-10</i>	21
<b>Studio clinico su 1179 impianti inseriti consecutivamente in un periodo di 5 anni</b> Cirotti B, Anelli B, Riccio G <i>Implant Tribune Italian Edition 2008; 1:13-14</i>	21
<b>Bone tissue engineering vs porous hydroxyapatite in maxillary sinus lift</b> Mangano C, Mangano F, Piattelli A, Macchi A, Mangano A, La Colla L <i>Italian Oral Surgery 2008; 4:45-59</i>	22
<b>Dense hydroxyapatite inserted into postextraction sockets. 20-year case report</b> Mangano C, Piattelli A, Perrotti V, Iezzi G <i>Journal of Periodontology 2008; 79(5):929-933</i>	22
<b>Histologic results from a human implant retrieved due to fracture 5 years after insertion</b> Iezzi G, Scarano A, Mangano C, Cirotti B, Piattelli A <i>Journal of Periodontology 2008; 79(1):192-198</i>	23
<b>Bone response to new modified titanium surface implants in non human primates</b> Mangano C, Perrotti V, Iezzi G, Scarano A, Mangano F, Piattelli A <i>Journal of Oral Implantology 2008; 34(1):17-24</i>	24
<b>Direct laser metal sintering as a new approach to fabrication of an isoelastic functionally graded material</b> Traini T, Mangano C, Sammons RL, Mangano F, Macchi A, Piattelli A <i>Dental Materials 2008; 24:1525-1533</i>	26
<b>The induction of bone formation by smart biphasic hydroxyapatite tricalcium phosphate biomimetic matrices</b> Ripamonti U, Richter PW, Nilen RWN, Renton L <i>Journal of Cellular and Molecular Medicine 2008; 12(6B):2609-2622</i>	28
<b><i>Impianti di titanio sinterizzati al laser</i></b> Mangano C, Macchi A, Mangano F, Piattelli A <i>Atti Congresso Nazionale Biomateriali 2008; 28-29</i>	
<b><i>Grande rialzo di seno utilizzando come sostituto osseo innesti custom made ottenuti da derivati naturali del corallo</i></b> Macchi A, Mangano C, Pozzi S <i>Atti Congresso Nazionale Biomateriali 2008; 43-44</i>	
<b>Self-inducing shape memory geometric cues embedded within smart hydroxyapatite-based biomimetic matrices</b> Ripamonti U, Richter PW, Thomas ME <i>Experimental 2007; 120(7):1796-1807</i>	29
<b>Studio morfologico di un impianto in titanio ottenuto per sinterizzazione tramite laser</b> Mangano C, Macchi A, Raspanti M, Mangano F <i>Dental Tribune 2007; 1:7</i>	
<b>Biological investigation of an experimental laser sintered titanium implant surface</b> Mangano F, Sammons RL, Mangano C, Montini S, Piattelli A <i>Clinical Oral Implant Research 2007; 18(5):333</i>	30

<b>Morphological investigation of an experimental laser sintered titanium implant</b> Raspanti M, Mangano C, Macchi A, Mangano F, Piattelli A, Traini T <i>European Journal of Implant Prosthodontics 2007; 1(3):28</i>	31
<b>Producing dental implants by Direct Laser Forming</b> Mangano C, Traini T, Piattelli A, Macchi A, Mangano F, Montini S, Mangano A <i>Italian Oral Surgery 2006; 4:7-12</i>	32
<b>Implanto-prosthetic treatment by means of Leader system</b> Mierzwinska-Nastalska E, Feder T, Spiechowicz E <i>Protet. Stomatol. 2006; 5:367-373</i>	32
<b>Bioengineering applied to osseointegrated implant dentistry: clinical reality or pure research?</b> Mangano C, Ripamonti U, Piattelli A, Mangano F, Montini S <i>Implantologia Orale 2006; 1:47-56</i>	33
<b>A new modified titanium implant surface: histological evaluation in non human primates and humans</b> Mangano C, Macchi A, Mangano A <i>Dental Horizon 2006; 4(2):313-317</i>	33
<b>Three dimensional custom made porous hydroxyapatite for bone regeneration</b> Mangano C, Macchi A, Mangano F, Montini S, Mangano A <i>Clinical Oral Implant Research 2006; 17(4):249</i>	34
<b>Histologic evaluation of immediately loaded titanium implants retrieved from humans</b> Mangano F, Mangano C, Piattelli A, Iezzi G, Perrotti V <i>Clinical Oral Implant Research 2006; 17(4):158</i>	35
<b>Surface microstructure and fibrin extension on titanium laser sintered specimens</b> Iezzi G, Traini T, Mangano C, Piattelli A <i>Journal of Clinical Periodontology 2006; 73-80</i>	35
<b>FESEM and microanalysis investigation of an experimental sintered titanium alloy implant</b> Iezzi G, Traini T, Mangano C, Sammons RL, Piattelli A <i>Academy of Osseointegration 21st Annual meeting 2006; 78</i>	36
<b>Implant prosthetic rehabilitation of elements with serious defect of bone tissue</b> Silvetti M, Gualerni Tognola P <i>Protech 2005; 4:29-37</i>	37
<b>Biomimetic surfaces and osseointegration: a study in non-human primates</b> Mangano C, Ripamonti U, Montini S, Mangano F <i>Italian Oral Surgery 2005; 2:9-17</i>	37
<b>Histologic evaluation of bone response to a new geometric surface configuration in non-human primates</b> Mangano C, Mangano F, Montini S <i>4th World Congress of Osseointegration 2004; In: Clinical Oral Implant Research</i>	38
<b>Implant geometric surface and osteogenesis. An histological study</b> Mangano C, Bartolucci E, Ripamonti U <i>Dental Cadmos 2003; 3:59-65</i>	39



### Scanning electron microscopy (SEM) and X-ray dispersive spectrometry evaluation of direct laser metal sintering surface and human bone interface: a case series

Scanning electron microscopy (SEM) and X-ray dispersive spectrometry evaluation of direct laser metal sintering surface and human bone interface: a case series

Mangano C, Piattelli A, Raspanti M, Mangano F, Cassoni A, Iezzi G, Shibli JA

**Lasers Medical Science**  
2011; 26:133–138

Recent studies have shown that direct laser metal sintering (DLMS) produces structures with complex geometry and consequently that allow better osteoconductive properties. The aim of this patient report was to evaluate the early bone response to DLMS implant surface retrieved from human jaws. Four experimental DLMS implants were inserted in the posterior mandible of four patients during conventional dental implant surgery. After 8 weeks, the micro-implants and the surrounding tissue were removed and prepared for scanning electron microscopy (SEM) and histomorphometric analysis to evaluate the bone-implant interface. The SEM and EDX evaluations showed a newly formed tissue composed of calcium and phosphorus. The bone-to-implant contact presented a mean of  $60.5 \pm 11.6\%$ . Within the limits of this patient report, data suggest that the DLMS surfaces presented a close contact with the human bone after a healing period of 8 weeks.

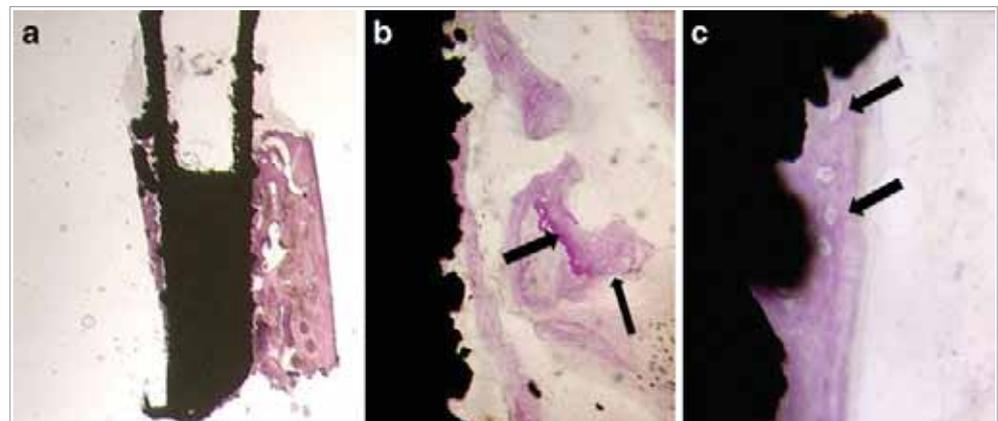


Fig. 4 a Histological ground section of the direct laser fabrication micro-implant surface after 8 weeks of healing depicting the newly formed bone showing early maturing stages. There are connecting bridges between the new bone trabeculae and the implant surface (basic fuchsin and toluidine blue staining, original 12x magnification).  
b There are reversal lines (arrows) between newly formed bone and the pristine bone (basic fuchsin and toluidine blue staining, original 100x magnification).  
c The newer bone tissue showing their osteocytes (arrows) is in close contact with the implant surface (basic fuchsin and toluidine blue staining, original 200x magnification).

## Early human bone response to laser metal sintering surface topography: a histologic report

Early human bone response to laser metal sintering surface topography: a histologic report

Mangano C, Piattelli A, D'Avila S, Iezzi G, Mangano F, Onuma T, Shibli JA

*Journal of Oral Implantology*  
2010; 36(2):91-96

This histologic report evaluated the early human bone response to a direct laser metal sintering implant surface retrieved after a short period of healing. A selective laser sintering procedure using a Ti-6Al-4V alloy powder with a particle size of 25–45 mm prepared this surface topography.

One experimental microimplant was inserted into the anterior mandible of a patient during conventional implant surgery of the jaw. The microimplant and surrounding tissues were removed after 2 months of unloaded healing and were prepared for histomorphometric analysis.

Histologically, the peri-implant bone appeared in close contact with the implant surface, whereas marrow spaces could be detected in other areas along with prominently stained cement lines. The mean of bone-to-implant contact was 69.51%.

The results of this histologic report suggest that the laser metal sintering surface could be a promising alternative to conventional implant surface topographies.



Fig. 4.(a) Histologic ground section of the direct laser fabrication microim-plant surface after 2 months of healing depicts the newly formed bone, showing early maturing stages. Connecting bridges can be seen between the new bone trabeculae and the implant surface (basic fuchsin and toluidine blue, original magnification x12). (b) A larger magnification of the lateral frame area in the section shown in (a). The arrows show the revers allines between newly formed bone and the pristine cortical bone (basic fuchsin and toluidine blue, original magnification x200).

Fig. 5. Histologic ground section depicts several osteocytes in their lacunae (arrows) in newly formed bone in the cement line (basic fuchsin and toluidine blue, original magnification x200).

## Influence of Direct Laser Fabrication Implant Topography on Type IV Bone: A Histomorphometric Study in Humans

Influence of Direct Laser Fabrication Implant Topography on Type IV Bone: A Histomorphometric Study in Humans

Shibli JA, Mangano C, D'Avila S, Piattelli A, Pecora GE, Mangano F, Iezzi G et al.

Journal of Biomedical Materials Research - Part A 2010; 93:607–614

**Purpose:** The aim of this histologic study was to evaluate the influence of a Direct Laser Fabrication (DLF) implant topography surface on bone-implant contact percentage (BIC%) as well as the bone density in the threads area (BD%) in type 4 bone after 2 months of unloaded healing.

**Materials and Methods:** 20 subjects (mean age = 42.6 years) were divided in test group (n= 10 patients - DLF implant surface topography) and control group (n=10 patients - sandblasted acid-etched surface) received 1 microimplant each during conventional implant surgery in the posterior maxilla. After a healing period of 2 months, the microimplants and the surrounding tissue were removed and prepared for ground sectioning and histomorphometric analysis.

**Results:** One microimplant with a sandblasted acid-etched surface was found to be clinically unstable at the time of retrieval. Histometric evaluation indicated mean BIC% was  $47 \pm 14.54\%$  and  $36.08 \pm 20.89\%$  for DLF and sandblasted acid-etched surfaces, respectively ( $p=0.03$ ). The BD% was similar for both surfaces ( $p>0.05$ ).

**Conclusions:** Within the limits of this study, the data suggest that the DLF implant topography presented a higher percentage of bone-implant contact compared with sandblasted acid etched surfaces, under unloaded conditions in posterior maxilla after a healing period of 2 months.

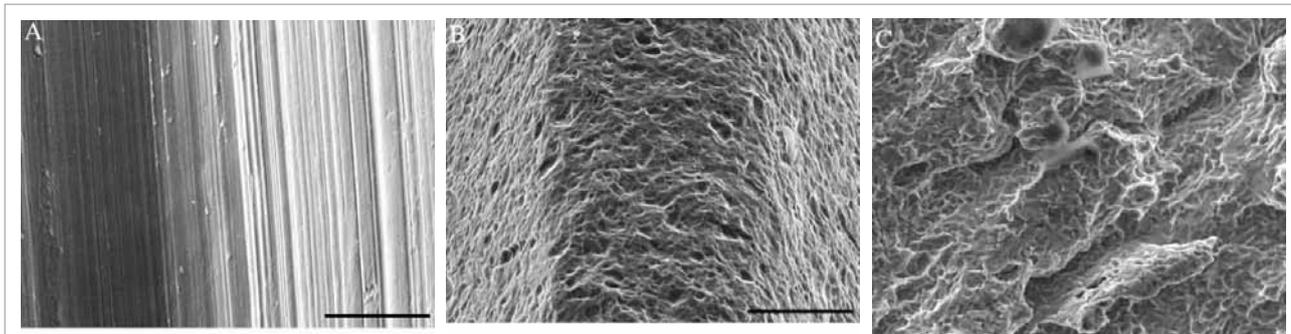


Figure 1. Scanning electron microphotograph of the (A) machined, (B) sandblasted acid-etched, and (C) direct laser fabrication surfaces (Barr = 50  $\mu\text{m}$ ).

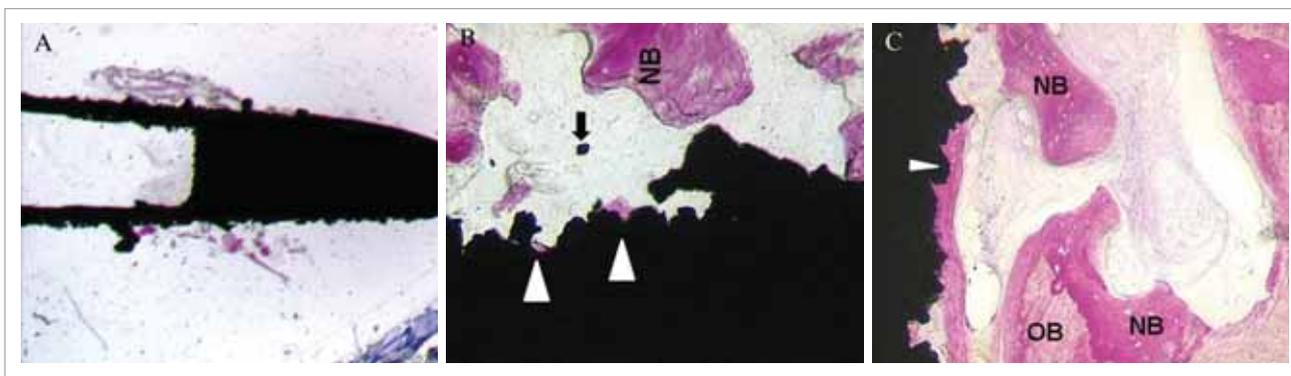


Figure 4. (A) Ground section of the direct laser fabrication surface (DLF) presenting newly-formed bone exhibited early stages of maturation and remodeling. (Basic fuchsin and toluidine blue staining, original magnification 312); (B) A thin layer of bone tissue (NB) in direct contact with DLF topography (arrow head) suggesting osteogenesis of contact. Particles inclusion could be detected (arrow); Basic fuchsin and toluidine blue staining, original magnification 3200); (C) Reversal lines separate the newly formed bone (NB) and pristine bone (OB). Arrow head depicts the contact osteogenesis next to implant surface.

## The osteoblastic differentiation of dental pulp stem cells and bone formation on different titanium surface textures

The osteoblastic differentiation of dental pulp stem cells and bone formation on different titanium surface textures

Mangano C, De Rosa A, Desiderio V, d'Aquino R, Piattelli A, De Francesco F, Tirino V, Mangano F, Papaccio G

**Biomaterials;**  
**2010; 31:3543-3551**

Bone Tissue Engineering (BTE) and Dental Implantology (DI) require the integration of implanted structures, with well characterized surfaces, in bone. In this work we have challenged acid-etched titanium (AET) and Laser Sintered Titanium (LST) surfaces with either human osteoblasts or stem cells from human dental pulps (DPSCs), to understand their osteointegration and clinical use capability of derived implants. DPSCs and human osteoblasts were challenged with the two titanium surfaces, either in plane cultures or in a roller apparatus within a culture chamber, for hours up to a month. During the cultures cells on the titanium surfaces were examined for histology, protein secretion and gene expression. Results show that a complete osteointegration using human DPSCs has been obtained: these cells were capable to quickly differentiate into osteoblasts and endotheliocytes and, then, able to produce bone tissue along the implant surfaces. Osteoblast differentiation of DPSCs and bone morphogenetic protein production was obtained in a better and quicker way, when challenging stem cells with the LST surfaces. This successful BTE in a comparatively short time gives interesting data suggesting that LST is a promising alternative for clinical use in DI.

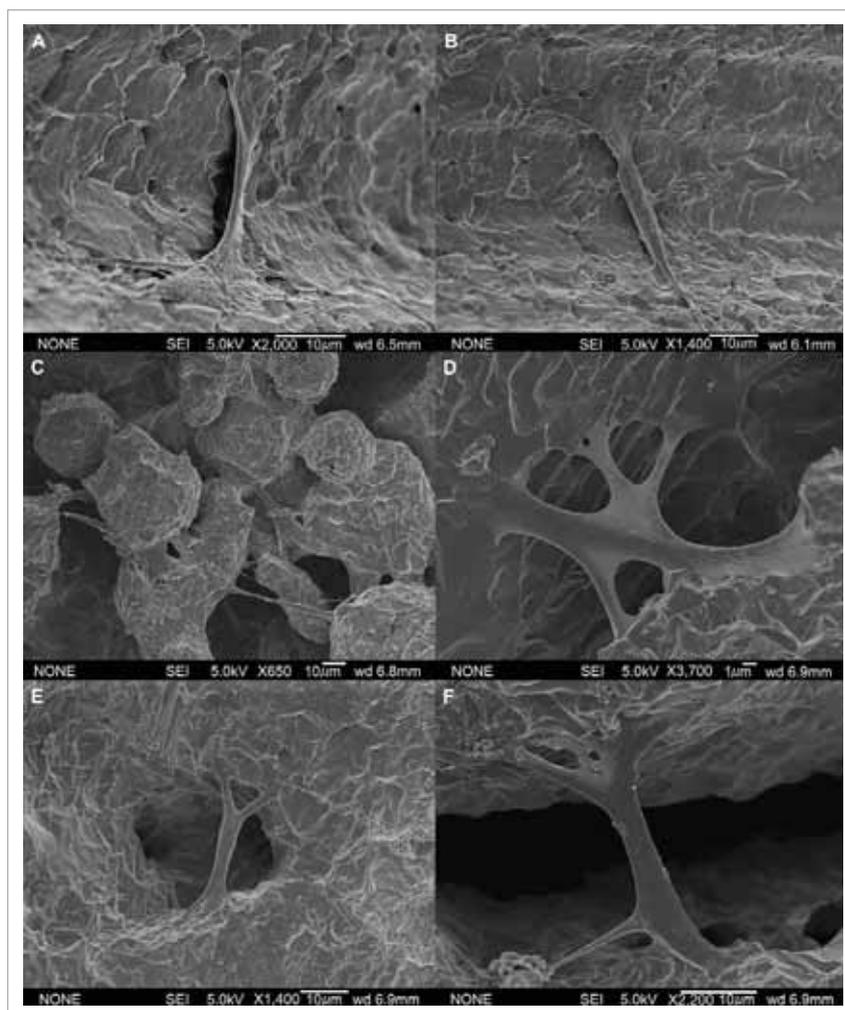


Fig. 2. Scanning Electron Microscope analyses of DPSCs and osteoblasts challenged, in culture, on titanium surfaces (AET=Acid-Etched Titanium; LST=Laser Sintered Titanium). The images show that, after a few hours of culture (4 or 8) osteoblasts (A) or DPSCs (B) on AET surfaces display a morphology indicating quiescent cells, while on LST surfaces those cells display better performances (C) (bars=10 $\mu$ m) and, in particular, DPSCs at 48 h (D) (bar=1 $\mu$ m) project several bridges and ramificate, leading the cells to a different morphology (E, F) (bars =10 $\mu$ m), typical of a differentiated osteoblast.

## A "custom-made" implant produced by microfusion of titanium particles: case report

A "custom-made" implant produced by microfusion of titanium particles: case report

Silvetti M, Mangano C,  
Macchi A, Mangano F

**Dental Cadmos:**  
2010; 78(7):133-142

**Objectives:** Modern technologies for the acquisition and conversion of radiographic images and specific software for creating 3D models can be used with Direct Laser Metal Forming (DLMF) technology to produce "custom-made" implants that are exact reproductions of the original radicular unit. This report describes a case that was successfully treated with an innovative implant protocol.

**Materials and methods:** The new protocol was used to treat a non-recoverable fracture of the second upper right premolar. Computed tomography images of the dento-radicular complex were acquired. With the aid of specific software, the images were elaborated to create a 3D model that was an exact copy of the root fragment that had to be extracted. Using laser sintering process and titanium micro-powders, we then created a "artificial root" implant based on the 3D model, which included an abutment for prosthetic rehabilitation (Silvetti-Combe method™). The tooth was extracted, and the "artificial root" was immediately inserted into the post-extraction socket and restored with a single crown.

**Results:** One year after the procedure, the "artificial root" seems to be perfectly integrated from both the functional and aesthetic points of view.

**Conclusions:** The possibilities to construct "custom-made" implants opens interesting new horizons in the field of modern prosthetic rehabilitation.



Fig. 5 "Artificial root" manufactured by DLMF technique



Fig. 8 Buccal and palatal fitting of the artificial root



Fig. 13 1year X-ray control

## Implant surface topography in modern implantology

### Part I: smooth and microrough surfaces

Implant surface topography  
in modern implantology  
Part I: smooth and microrough  
surfaces

Mangano F, Mangano C, Macchi A,  
Perrotti V, Iezzi G, Piattelli A

**Italian Oral Surgery:**  
2010; 9(4):201-214

**Objectives:** To analyse the influence of implant surfaces on bone healing. In this first part, smooth and microrough surfaces are analyzed in detail, while in the second part nanostructured and DLF (Direct Laser Fabrication) surfaces are taken into consideration.

**Materials and methods:** By the extensive literature review, the fundamental aspects of bone healing are taken into consideration, and traditional implant surfaces are described, showing limits and advantages of both smooth and rough implant surfaces. Several techniques to obtain different implant surface topographies are examined.

**Results and conclusions:** Modern implant dentistry aims at early and immediate loading, and implant surface topography, with its micro- and ultrastructural aspects, represents a key factor to achieve osseointegration. At present, implants with a microrough surface seem to promote a faster and greater new bone apposition when compared with smooth implants.

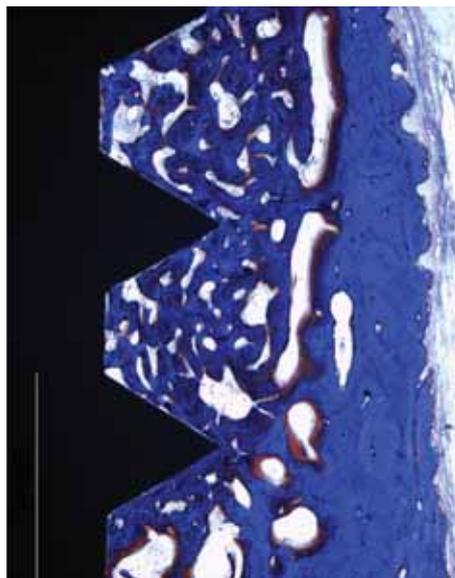


Fig. 4 Organic acid etched surface. Bone formation on implant surface, with bone growth inside cavities (Goldner three-chrome colour 200X).

## Implant surface topography in modern implantology Part II: nanostructured and DLF surfaces

Implant surface topography  
in modern implantology  
Part II: nanostructured and  
DLF surfaces

Mangano F, Mangano C, Macchi A,  
Perrotti V, Iezzi G, Piattelli A

**Italian Oral Surgery:**  
2010; 9(5):261-262, 265-275

**Objectives:** To analyze the influence of implant surfaces on bone healing processes. In the first part of this article, smooth and microrough surfaces were analyzed, while in the second part nanostructured and DLF (Direct Laser Fabrication) surfaces are discussed.

**Materials and methods:** By an extensive literature review, the fundamental aspects of bone healing processes are taken into consideration. Recently, many implant surfaces with nanotopographical features obtained with different techniques have been marketed. A new method to produce dental implants by laser fusion of titanium microparticles is described as well.

**Results and conclusions:** Modern implant dentistry aims at early and immediate functional loading, and implant surface topography, with its micro- and ultrastructural aspects, is a key factor for achieving osseointegration. Nanostructured surfaces can modify tissue response, enhancing osteoblasts adhesion. The DLF technique allows to create a dental implant by modifying the density and porosity of different layers, thus supporting better load adaptation and bone integration.

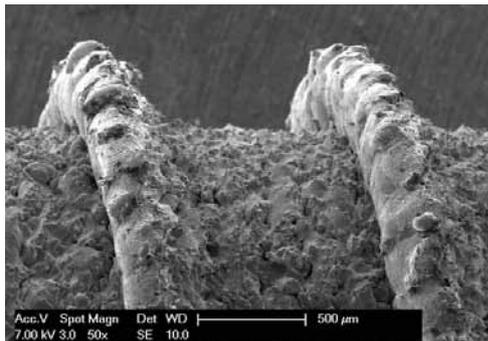


Fig. 3 Direct Laser microfused titanium surface. At higher magnification the surface porosity (SEM, 50X).

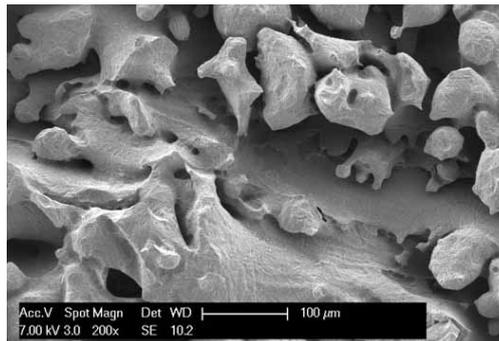


Fig. 4 Direct Laser microfused titanium surface. At higher magnification the interconnected pores (SEM, 200X).

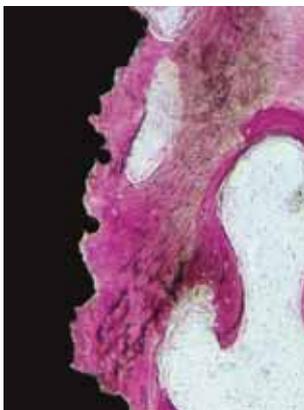


Fig. 5 Direct Laser microfused titanium surface. Compact bone with marrow spaces in contact with the implant surface (Toluidine blue and acid fuchsine 200X).

## Immediate loading of modified acid etched dental implants in post-extraction sockets

Immediate loading of modified acid etched dental implants in post-extraction sockets: a histological and histomorphometrical comparative study in non-human primate *Papio Ursinus*

Mangano C, Piattelli A, Mangano F, Perrotti V, Iezzi G

**Implant Dentistry**  
2009; 18(2):142-150

**Purpose:** Immediate loading of dental implants inserted into fresh post-extraction sites has recently been proposed as a novel but challenging surgical approach. However, histological evidence and comparative data are still missing. The aim of this study was an histological and histomorphometrical comparison of submerged and immediately loaded dental implants with a new modified acid etched surface inserted into post extraction sites of non-human primates.

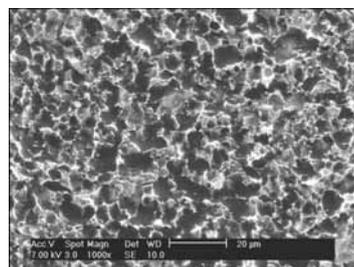
**Materials and Methods:** Thirty-two implants were placed in post-extraction sockets of 4 adult Chacma Baboons (*Papio Ursinus*). Each baboon received 8 implants: four submerged and four immediately loaded. The implants were retrieved after 90 days of healing with a 4 mm trephine bur and processed for histology and histomorphometry.

**Results:** The bone-to-implant contact percentage in the submerged and immediate loaded implants was 86.02 and 86.85 %, respectively, with no statistically significant differences. In the immediately loaded implants a greater amount of ongoing remodelling was observed.

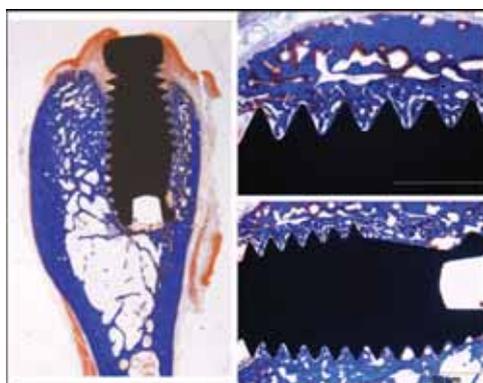
**Conclusions:** Immediate loading seemed to be a valid alternative to conventional technique when a implant is inserted into post-extraction sockets. Further comparative studies on a greater number of samples are necessary to confirm our findings.



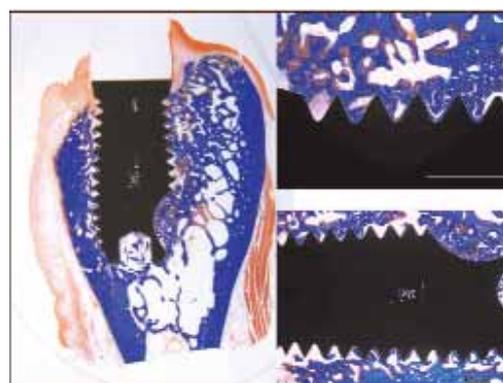
Postextraction implants inserted in the left mandible of baboons. Cover screws were positioned and mucosa sutured over the implants.



SEM image of acid-etched modified implant surface.



Submerged implant. It is possible to observe the formation of bone around the implant surface. A large portion of the implant perimeter is covered by bone. At higher magnification (inset), a close connection between bone and implant surface is present.



Immediately loaded implant. A large part of the implant surface is covered by bone. At higher magnification (inset), bone is in tight connection with the implant surface.

## Dental implants from laser fusion of titanium microparticles: from research to clinical applications

Impianti dentali ottenuti dalla fusione di microparticelle di titanio tramite laser: dalla ricerca alla clinica

Mangano C, Shibli JA, Mangano F  
Sammons RL, Macchi A

**Journal of Osseointegration**  
2009; 1(1):9-22

Dental implants currently available on the market are conventionally produced by machining titanium rods, with subsequent application of surface treatments or coatings, with the aim to accelerate bone healing process.

The progress in the field of rapid prototyping technology makes possible to modulate the elastic properties of the implants to those of surrounding bone.

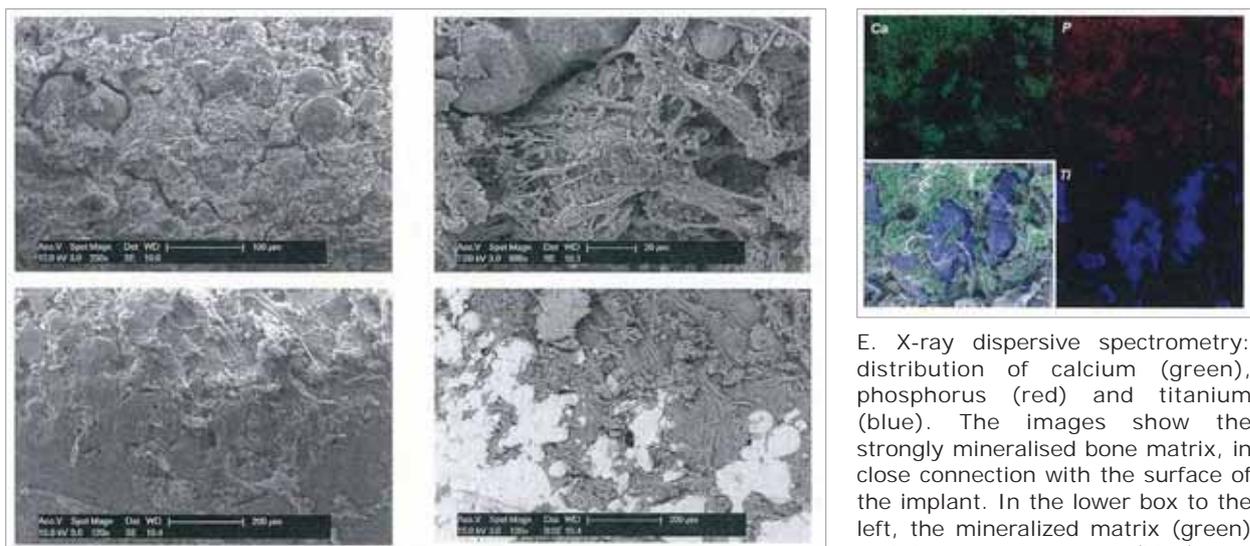
The direct laser fabrication (DLF) allows solids with complex geometry to be produced by focusing metal powder microparticles in a laser beam, according with a computer three-dimensional (3D) model. For dental implants, the fabrication process involves the fusion, through a computer guided laser beam, of titanium microparticles, in order to realise, layer by layer (20 micron thick each one) the desired object.

Our Research Group, first in the world, has invented a method for production of dental implants obtained from laser fusion of titanium microparticles. With our method it is possible to create, regulating the settings of the different layers, implants with graduated and controlled porosity, incorporating a gradient of porosity, from the inner core to the outer surface.

On the one hand, this kind of modulation can allow a better load adaptation and distribution; on the other hand, the new porous surface can promote the bone healing process.

The new implants obtained from the fusion of titanium microparticles show a surface with a repetitive sequence of concavities, which are directly connected to the underlying porous spaces. This kind of geometry, rich in interconnected pores, has demonstrated in previous works a good biological response *in vitro*.

The aim of the present study was to test the biological behaviour of the new implants obtained from the fusion of titanium microparticles (TiXOs, Leader-Novaxa, Milan, Italy) *in vivo*, in human type IV bone, after an unloaded healing period of two months.



DLMF surface. A. Scanning electron microscopy of the mineralized bone matrix on the implant surface. B. At higher magnification, the bone matrix results in close connection with the implant surface. C. The bone matrix is evidenced inside the concavities and irregular grooves of the implant surface. D. Electronic backscattered: this technique allows you to easily distinguish the bone (dark) from the metal surface (clear).

E. X-ray dispersive spectrometry: distribution of calcium (green), phosphorus (red) and titanium (blue). The images show the strongly mineralised bone matrix, in close connection with the surface of the implant. In the lower box to the left, the mineralized matrix (green) and the titanium surface (blue).

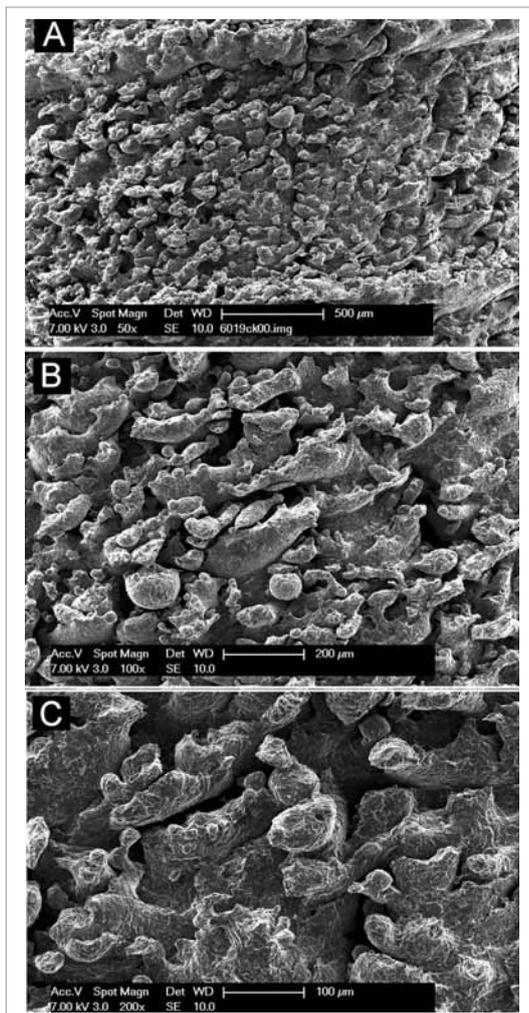
## Stereo imaging and cytocompatibility of a model dental implant surface formed by direct laser fabrication

Stereo imaging and cytocompatibility of a model dental implant surface formed by direct laser fabrication

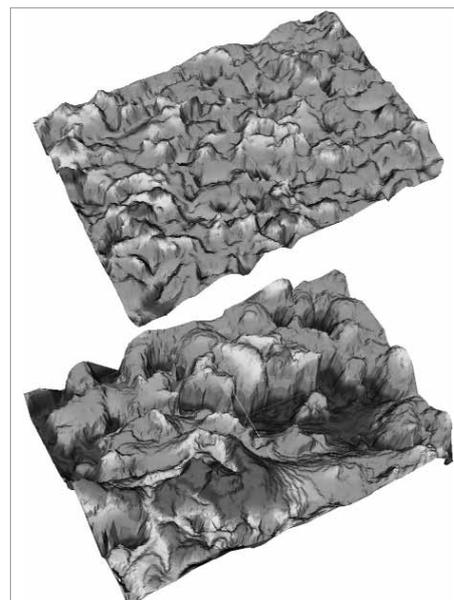
Mangano C, Raspanti M, Traini T, Sammons RL, Piattelli A

Journal of Biomedical Materials Research - Part A  
2009; 88A(3):823-831

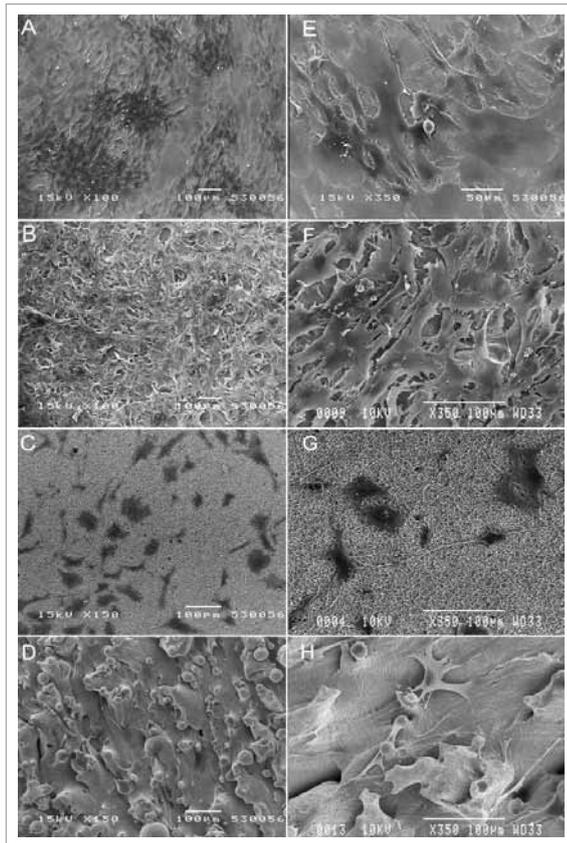
Direct laser fabrication (DLF) allows solids with complex geometry to be produced by sintering metal powder particles in a focussed laser beam. In this study ten Ti6Al4V alloy model dental root implants were obtained by DLF and surface characterization was carried out using stereo scanning electron microscopy to produce a 3D reconstructions. The surfaces were extremely irregular, with approximately 100  $\mu\text{m}$  deep, narrow intercommunicating crevices, shallow depressions and deep, rounded pits of widely variable shape and size, showing ample scope for interlocking with the host bone. Roughness parameters were:  $R_t$ , 360.8  $\mu\text{m}$ ;  $R_z$ , 358.4  $\mu\text{m}$ ;  $R_a$ , 67.4  $\mu\text{m}$  and  $R_q$ , 78.0  $\mu\text{m}$ . Disc specimens produced by DLF with an identically prepared surface were used for biocompatibility studies with rat calvarial osteoblasts: After 9 days cells had attached and spread on the DLF surface, spanning across the crevices and voids. Cell density was similar to that on a commercial rough microtextured surface but lower than on commercial smooth machined and smooth-textured grit-blasted, acid etched surfaces. Human fibrin clot extension on the DLF surface was slightly improved by organic acid etching to increase the micro-roughness. With further refinements DLF could be an economical means of manufacturing implants from titanium alloys.



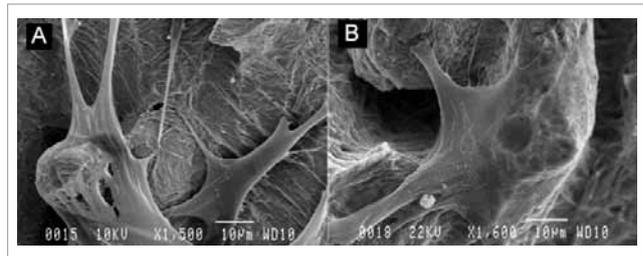
A: Low-magnification scanning electron micrograph of the surface of a metal implant. The superficial texture appears uniformly jagged across the whole field of view. B: At higher magnification the alternation of rounded features, narrow crevices and deep indents is particularly evident. The hollows extend beneath the visible surface in articulated undercuts. C: At 200X and above the crystalline structure of the metal becomes prevalent. The surfaces never show contamination traces and appear entirely made of solid metal.



A colour-mapped, false-colour rendering of two 3D reconstructions from micrographs taken at 50X (above) and 200X (below). The 3D texture of the surface is readily evident and quite consistent with conventional SEM micrographs.



Comparison of cell density and morphology on DLF discs after 9 days. A–D: 100–150X magnification; (E–H) 350X magnification; (A,E) smooth machined surface; (B,F) DPS<sup>®</sup>; (C,G) Plus<sup>®</sup>; (D,H) DLF surface. Scale bars=100µm.



Higher magnification of images of cells shown in Fig. 5 on the DLF surface [(A) 1500x and (B) 1600x] showing attachment to the surface. Scale bar=10µm.

## Two modifications of maxillary sinus lift technique

Two modifications of maxillary sinus lift technique

Rapani C, Rapani M

**Italian Oral Surgery**  
2009; 8(3):127-134

**Objectives:** To propose two modifications of lateral standard technique for maxillary sinus lift that make it easier and allow to put filling material even in case of wide lacerations. That could be otherwise untreatable.

**Materials and Methods:** After a brief literature review about the most frequently used techniques for maxillary sinus lift and basic operative knowledge needed, two surgical modifications are shown.

**Results:** The authors report their experience about maxillary sinus lift acquired in 7 years of surgical practice: 246 interventions, including 45 maxillary sinus lift with occlusal access and 201 with lateral access, with immediate or delayed implant insertion. Follow up lasted at least one year, while 150 patients were followed 9 months and 17 years.

## Direct metal laser-sintering per la produzione di impianti "custom made"

Direct metal laser-sintering per la produzione di impianti "custom made"

Macchi A, Taubert Pozzi S, Zecca PA

**DoctorOS**  
2009; 8:1086-1087

La tecnologia Direct metal laser-sintering (DMLS) permette di ottenere strutture complesse in metallo a partire da file CAD realizzandole, per addizione strato su strato, mediante un fascio laser che sinterizza le nanoparticelle di metallo. Questa metodica è già da diversi anni in uso in molteplici settori produttivi (aeronautica, meccanica) e si sta velocemente diffondendo anche in campo odontoiatrico.

Il titanio utilizzato comunemente per la produzione di impianti dentali possiede ottime caratteristiche di biocompatibilità e di resistenza meccanica, tuttavia ha un'elasticità inferiore a quella dell'osso, causando stress meccanici nella zona circostante l'impianto.

Oggi, mediante sinterizzazione laser, è possibile produrre impianti personalizzati utilizzando la polvere di titanio (Ti-6Al-4V) come materiale di partenza. Il processo avviene in un ambiente saturo di gas argon, tramite un sistema con una sorgente di Ytterbium laser da 200W, capace di costruire oggetti con una precisione di 20 micron e fino ad un volume di 250 mm x 250 mm x 215 mm. L'apparecchiatura EOSINT è stata messa a disposizione da Leader Italia (Cinisello Balsamo, Milano).

Gli impianti in titanio ottenuti presentano una struttura ruvida e porosa, costituita da particelle di dimensione compresa tra 5 e 50 micron; gli stessi quindi si adattano molto bene alle proprietà elastiche dell'osso minimizzando lo stress e migliorando la prognosi a lungo termine.

## The induction of bone formation by coral-derived calcium carbonate/hydroxyapatite constructs

The induction of bone formation by coral-derived calcium carbonate/hydroxyapatite constructs

Ripamonti U, Crooks J, Khoali L, Roden L

**Biomaterials**  
2009; 30:1428-1439

The spontaneous induction of bone formation in heterotopic rectus abdominis and orthotopic calvarial sites by coral-derived biomimetic matrices of different chemical compositions was investigated in a long-term study in the non-human primate *Papio ursinus*. Coral-derived calcium carbonate constructs were converted to hydroxyapatite by hydrothermal exchange. Limited conversion produced hydroxyapatite/calcium carbonate (HA/CC) constructs of 5% and 13% hydroxyapatite. Rods of 20 mm in length and 7 mm in diameter were implanted in heterotopic rectus abdominis sites: discs 25 mm in diameter were implanted in orthotopic calvarial defects of six adult non-human primates *P. ursinus*. Heterotopic samples also included fully converted hydroxyapatite replicas sintered at 1100°C. To further enhance spontaneous osteoinductive activity, fully converted hydroxyapatite replicas were coated with the synthetic peptide P15 known to increase the adhesion of fibroblasts to anorganic bovine mineral. Bone induction was assessed at 60, 90 and 365 days by histological examination, alkaline phosphatase and osteocalcin expression, as well as by expression of BMP-7, GDF-10 and collagen type mRNAs. Induction of bone occurred in the concavities of the matrices at all time points. At 365 days, bone marrow was evident in the P15-coated and uncoated implants. Resorption of partially converted calcium carbonate/hydroxyapatite was apparent, as well as remodeling of the newly formed bone. Northern blot analyses of samples from heterotopic specimens showed high levels of expression of BMP-7 and collagen type IV mRNA in all specimen types at 60 days, correlating with the induction of the osteoblastic phenotype in invading fibrovascular cells. Orthotopic specimens showed prominent bone formation across the different implant constructs. The concavities of the matrices biomimeticize the remodeling cycle of the osteonic primate cortico-cancellous bone and promote the ripple-like cascade of the induction of bone formation. This study demonstrates for the first time that partially converted HA/CC constructs also induce spontaneous differentiation of bone, albeit only seen one year post-implantation.

## Combining scaffolds and osteogenic cells in regenerative bone surgery

Combining scaffolds and osteogenic cells in regenerative bone surgery

Mangano C, Piattelli A, Mangano A, Mangano F, Mangano A, Iezzi G, Borges F, D'Avila S, Shibli JA

**Clinical Implant Dentistry and Related Research**  
2009; 11(S1):92-102

**Purpose:** The following case series evaluated the maxillary sinus augmentation responses to tissue-engineered bone graft obtained by a culture of autogenous osteoblasts seeded on polyglycolic-polylactic scaffolds and calcium phosphate.

**Materials and Methods:** Sinus floor augmentation was performed bilaterally in five patients (mean age 58.4 years) with tissue-engineered bone (test site - Oral Bone®, BioTissue, Freiburg, Germany) or calcium phosphate (control site - Biocoral, Novaxa SpA, Milan, Italy). Biopsies were harvested 6 months after sinus augmentation for histometric evaluation. Volumetric measurements were taken at baseline and 6 months after the surgical procedure.

**Results:** The mean of vertical bone gain was 6.47 +/- 1.39 and 9.14 +/- 1.19 mm to test and control sites, respectively. The histological sections depicted mature bone with compact and cancellous areas. All biopsies contained varying percentages of newly formed bone and marrow spaces. The mean of bone tissue in the grafted area was 37.32 +/- 19.59 % and 54.65 +/- 21.17 % for tissue-engineered bone and calcium phosphate, respectively.

**Conclusion:** Within the limits of the present report, the histological data in humans confirmed that tissue-engineered bone and calcium phosphate allowed newly formed bone after maxillary sinus augmentation.

***Early human bone response to laser metal sintering surface topography: a histologic evaluation***

*Early human bone response to laser metal sintering surface topography: a histologic evaluation*

Shibli JA, Mangano C, Mangano F, Iezzi G, Cardoso L, Onuma T, Ferrari D, Piattelli A

*Clinical Oral Implant Research*  
2009; 20(9):1036

**Background and aim:** Earlier studies have shown that direct laser metal sintering (DLMS) technique produces structures with complex geometry that allow better osteoconductive properties. The aim of this study was to evaluate the influence of the DLMS topography on bone-to-implant contact (BIC%), on bone density in the threaded area (BA%) as well as bone density outside the threaded area (BD%) in type IV bone after 8 weeks of unloaded healing.

**Materials and methods:** Thirty patients (mean age  $51.34 \pm 3.06$  years) received one micro-implant (2.5 mm diameter and 6 mm length) each during conventional implant surgery in the posterior maxilla. Thirty micro-implants with three topographies were evaluated: 10 machined (cpTi); 10 sandblasted and acid etched surface (SAE) and 10 DLMS micro-implants. DLMS surface topography was prepared by a selective laser sintering procedure using a Ti-6Al-4V alloy powder with a particle size of 1-10  $\mu$ m. After 8 weeks, the micro-implants and the surrounding tissue were removed and prepared for histomorphometric analysis.

**Results:** Four micro-implants (2cpTi, 1SAE and 1DLMS) showed no osseointegration after the healing period. Histometric evaluation indicated that the mean BIC% was higher for the DLMS and SAE surfaces ( $P \leq 0.0002$ ). The BA% was higher for the DLMS surface, although there was no difference with the SAE surface. The BD% was similar for all topographies ( $P > 0.05$ ).

**Conclusion:** Data suggest that the DLMS and SAE surfaces presented a higher bone-to-implant contact rate compared with cpTi surfaces under unloaded conditions, after a healing period of 8 weeks.

### *Histomorphometric and torque out evaluation of new laser treated implant surfaces*

*Histomorphometric and torque out evaluation of new laser treated implant surfaces: an in vivo study on ovine iliac crest*

*De Benedictis S, Berardi D, Malagola C, Trisi P, Perfetti G*

*Clinical Oral Implant Research*  
2009; 20(9):1028

**Background and aim:** Implant surface roughness and purity play a fundamental role in the osseointegration process. Common methods of roughness production generate irregular and unrepeatable surface patterns, and even contaminate implant surfaces with materials other than titanium which could interfere with the osseointegration process. On the other hand, laser engineering allows to preset those parameters which will determine implant roughness, in order to generate micrometric porosities repeatable in their shape, diameter and depth, as well as in their distribution and pitch. In addition, any contact between surface and the operating tools is avoided resulting in total absence of contaminants such as silica and aluminum. These particles, could have proinflammatory effects. The aim of this study is to carry out, in an animal model, a histomorphometric and biomechanic comparative evaluation between 20 and 30 laser implants and machined implants.

**Materials and methods:** Sample implants have a diameter of 3.8 mm and a length of 9 mm. 44 implants were inserted: 28 with half laser and half machined surface, seven with total laser surface, nine with total machined surface. They were placed in the iliac crest of five Bergamasca sheep, with an average weight of 60 kg, at the end of their scheletric growth. Animals were sacrificed 8 weeks after surgery, by an intravenous injection of Tanax (10 cm<sup>3</sup>). On all bone specimens histologic and histomorphometric analysis were estimated. On total laser and total machined implants, even biomechanical tests were carried out. On obtained data, a statistical analysis was performed.

**Results:** Biomechanical results show how the average Torque-out value of total laser implants are up to three times higher than machined implants value. Histomorphometric results demonstrate statistically significant differences ( $P < 0.0001$ ) in favour of laser surfaces.

**Conclusion:** In this study, histologic, histomorphometric and biomechanical results show how laser surface engineering is a viable method to obtain high superficial purity and an extremely regular and repeatable surface micromorphology, able to give a positive influence to bone cell response and to enhance osseointegration percentage value.

## Cellule staminali adulte: una nuova frontiera nella rigenerazione ossea in Odontostomatologia

Cellule staminali adulte: una nuova frontiera nella rigenerazione ossea in Odontostomatologia

Mangano F, Mangano C, Macchi A, Piattelli A, Montini S

**Implant Tribune Italian Edition**  
2008; 1:1-10

L'Ingegneria Tessutale Ossea promette, attraverso la combinazione di tre elementi fondamentali quali biomateriali, fattori di crescita e cellule osteogeniche, di ottenere il materiale d'innesto ideale in chirurgia ossea rigenerativa, con tutte le desiderabili caratteristiche dell'osso autologo, senza limiti di disponibilità quantitativa. In particolare, l'utilizzo di biomateriali in combinazione con cellule staminali rappresenta una delle sfide più avvincenti nell'ambito dell'Ingegneria Tessutale Ossea. La recente scoperta della presenza di cellule staminali nei tessuti dell'adulto ha aperto una nuova strada, ed oggi è possibile prelevare, isolare, espandere e differenziare queste cellule, seminarle su biomateriale ed innestarle in difetti ossei. L'impiego di matrici strutturalmente e biologicamente adeguate a veicolare l'attività cellulare rappresenta un requisito imprescindibile; la geometria superficiale del substrato, in particolare, riveste un ruolo di grande importanza, in quanto è in grado di determinare specifiche risposte cellulari.

## Studio clinico su 1179 impianti inseriti consecutivamente in un periodo di 5 anni

Studio clinico su 1179 impianti inseriti consecutivamente in un periodo di 5 anni

Cirotti B, Anelli B, Riccio G

**Implant Tribune Italian Edition**  
2008; 1:13-14

Da quando, circa venticinque anni fa, Branemark dettò i parametri della moderna implantologia, numerosi studi ne hanno confermato la validità clinica e scientifica, al punto che oggi tale metodica è entrata nella routine ambulatoriale a pieno titolo, divenendo in molti casi la prima scelta nella riabilitazione delle edentule umane.

Le acquisizioni scientifiche degli ultimi anni hanno modificato i protocolli chirurgici originali di Branemark ed i nuovi trattamenti di superficie hanno, inoltre, accelerato i tempi di carico protesico, con notevoli vantaggi per i pazienti sia sotto il profilo della morbilità che dal punto di vista estetico.

La continua evoluzione delle superfici dei sistemi implantari, la migliore conoscenza da parte dei clinici delle procedure di diagnosi e una più accurata valutazione dei protocolli relativi ai piani di trattamento, hanno portato ad una più elevata predicibilità della terapia impiantare, con maggiori percentuali di successo nel lungo periodo.

Nella maggior parte delle pubblicazioni presenti in letteratura, viene valutato il grado di successo impiantare prendendo in considerazione solo gruppi omogenei di pazienti, scartando spesso dalle statistiche i fumatori e considerando solo gli impianti inseriti in osso sano.

Scopo di questo studio è analizzare il comportamento clinico e la sopravvivenza a cinque anni di impianti (Leader Italia - Milano) con una nuova superficie, ottenuta mediante trattamento con una miscela di acidi organici che produce una morfologia uniforme, caratterizzata da micro e macroconcavità. Tale valutazione viene fatta indipendentemente dalla morfologia ossea, dalle tecniche chirurgiche e dalle abitudini del paziente.

Bone tissue engineering vs hydroxyapatite in maxillary sinus lift

Mangano C, Mangano F, Piattelli A, Macchi A, Mangano A, La Colla L

**Italian Oral Surgery**  
2008; 4:45-59

### Bone tissue engineering vs porous hydroxyapatite in maxillary sinus lift

Modern bone tissue engineering techniques are expected to allow bone regeneration in difficult cases thanks to a combination of biomaterials and osteogenic cells without harvesting autologous bone.

The aim of this work is to compare vertical bone gain obtained in maxillary sinus augmentation with an engineered bone graft transplant, made of human autologous osteoblasts grown over polyglycol-poly lactid (PLGA) scaffolds (Oral Bone®, Biotissue, Freiburg, Germany) versus coral derived porous hydroxyapatite (Biocoral®, Novaxa SpA, Milano, Italia), in 5 patients that have undergone a bilateral maxillary sinus elevation.

Radiographical comparative analysis (CT) before and 6 months after surgery has revealed a significantly greater vertical bone gain ( $P=0.05$ ) within sinuses treated with porous hydroxyapatite only.

### Dense hydroxyapatite inserted into postextraction sockets. A histologic and histomorphometric 20-year case report

Dense hydroxyapatite inserted into postextraction sockets. A histologic and histomorphometric 20-year case report

Mangano C, Piattelli A, Perrotti V, Iezzi G

**Journal of Periodontology**  
2008; 79(5):929-933

**Background:** The biological behavior, i.e. the degradation of hydroxyapatite (HA) in the human body, is certain of relevance for clinicians. The aim of the present investigation was a long-term (20 years) histologic and histomorphometric evaluation of dense HA used in post-extraction sockets.

**Methods:** Dense HA particles were used in post-extraction alveolar sockets, in a patient, to maintain the alveolar ridge height. The patient came again to our observation after 20 years for implant treatment. During implant insertion surgery a ridge remodeling was necessary and the HA/bone tissue was harvested with bone cutting forceps from canine and premolar area. The specimen was processed for histology and histomorphometry at the Implant Retrieval Centre, Dental School, University of Chieti-Pescara, Italy.

**Results:** Most of the particles (56%) were partially surrounded, while some particles (39%) were completely surrounded by bone. At higher magnification, bone was in close contact with the particles and neither gaps or fibrous tissues were present at the bone-biomaterial interface. Microscopically, the particles had a dense appearance. Only in a few fields it was possible to observe some HA particles that had detached from the particles' surface. Histomorphometry showed that bone represented 25.4 %  $\pm$  3.2 %, marrow spaces 41.3 %  $\pm$  5.2 % and residual HA particles 38.1 %  $\pm$  4.1 %.

**Conclusions:** Intimate binding between bone and the particles of HA was present even after a long-term implantation period (20 years). The fact that HA particles were closely surrounded by bone was very promising for the long-term stability of the augmentation.

## Histologic results from a human implant retrieved due to fracture 5 years after insertion

Histologic results from a human implant retrieved due to fracture 5 years after insertion with anorganic bovine bone

Iezzi G, Scarano A, Mangano C, Cirotti B, Piattelli A

**Journal of Periodontology**  
2008; 79(1):192-198

**Background:** Little is known about the healing pattern and the osseointegration processes at the interface of implants placed in different grafting materials in man. Anorganic bovine bone is a xenogenic material with a high biocompatibility and osteoconductivity.

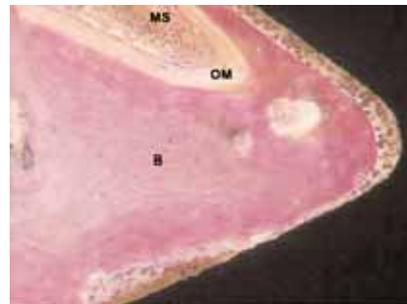
**Methods:** A 47-year-old patient underwent a monolateral sinus augmentation procedure. For the graft procedure 100% anorganic bovine bone was used. Two titanium dental implants with an acid-etched surface (Leader Italia implants) were inserted at the same time of the grafting procedure. After 6 months, a fixed prosthetic restoration was placed. After a 5 years loading period, the mesial implant fractured and the implant was removed with a 5 mm trephine bur.

**Results:** At low magnification, the bone appeared to be trabecular and in the peri-implant bone, many particles of anorganic bovine bone were still present. Between the anorganic bovine bone particles and the metal surface there was always the interposition of bone, and in no case the graft particles were in contact with the implant. No acute or chronic inflammatory cell infiltrate or foreign body reaction were present around the particles or at the bone-implant interface. The tissues around the implant were composed by  $40 \pm 2.4$  % of bone, by  $12 \pm 2.9$  % of anorganic bovine bone particles, and by  $50 \pm 6.2$  % of marrow spaces. The percentage of bone-to-implant contact was  $48.6\% \pm 3.7\%$ .

**Conclusions:** A high percentage (~50%) of direct contact between bone and implant, without the interposition of graft material particles was present. ABB had enabled implant integration to take place, which had remained stable for 5 years.



Low-power magnification showing bone around the implant perimeter (acid fuchsin-toluidine blue; original magnification X6).



Bone found at the interface of the implant. Extravasated red blood cells can be seen at the interface. (Acid fuchsin-toluidine blue; original magnification X100). OM=osteoid matrix, B=bone; MS=marrow space.

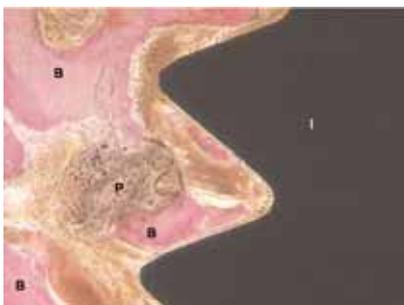


ABB particle surrounded by bone and distant from the implant surface. Extravasated red blood cells are seen at the interface and in the marrow spaces. (Acid fuchsin-toluidine blue; original magnification X40). B=bone; P=particle; I=implant.



Two particles separated from the implant surface by bone. Arrows point to osteoblasts. (Acid fuchsin-toluidine blue; original magnification X100). WB=woven bone; P=particle; CT=connective tissue; I=implant.

## Bone response to new modified titanium surface implants

Bone response to new modified titanium surface implants in nonhuman primates (*Papio ursinus*) and humans: histological evaluation

Mangano C, Perrotti V, Iezzi G, Scarano A, Mangano F, Piattelli A

*Journal of Oral Implantology*  
2008; 34(1):17-24

**Purpose:** The aim of this study was a comparative histological and histomorphometrical evaluation of the effect on early bone formation of two different implant surfaces: a machined and a new acid-etched implant surface (Leader s.r.l. Milano–Italy)

**Materials and methods:** Ten screw-type microimplants were placed in 5 patients. Each patient received 2 microimplants (2 mm in diameter and 5 mm in length): one with a machined surface (control) and one with an acid-etched surface (test). The microimplants were retrieved after 60 days of healing with a 4 mm trephine bur and processed for histology. Moreover, 24 regular size implants, 12 with a machined surface (control) and 12 with an acid-etched surface (test) were placed in 2 adult non-human primates, 3 months after the extraction of premolars and molars. Each animal received three machined implants (control) in the right hemi mandible and three acid-etched implants (test) in the left hemi mandible. The same animals received 3 control implants and three test implants in the rectus abdomen muscle. After 1 months, the implants were retrieved from the mandible and the rectum abdomen muscle and processed for histology.

**Results:** Histomorphometric evaluation demonstrated a higher bone-to-implant contact in the test implants compared with the controls, in both primates (25,55% vs 15,8%) and humans (62% vs 45%). Moreover, in non-human primates after 1 months of healing it was possible to observe a poor osseointegration in the control specimens, while newly-formed bone in direct contact with test implants was evident. The rectus abdomen specimens showed that the acid-etched surfaces can stimulate the formation and attachment of new connective and vascular tissues more than machined surfaces.

**Conclusions:** Implant surface geometry can speed up bone formation creating a special microenvironment which promotes angiogenesis. Long-term studies are needed to test further this new acid-etched implant surface.

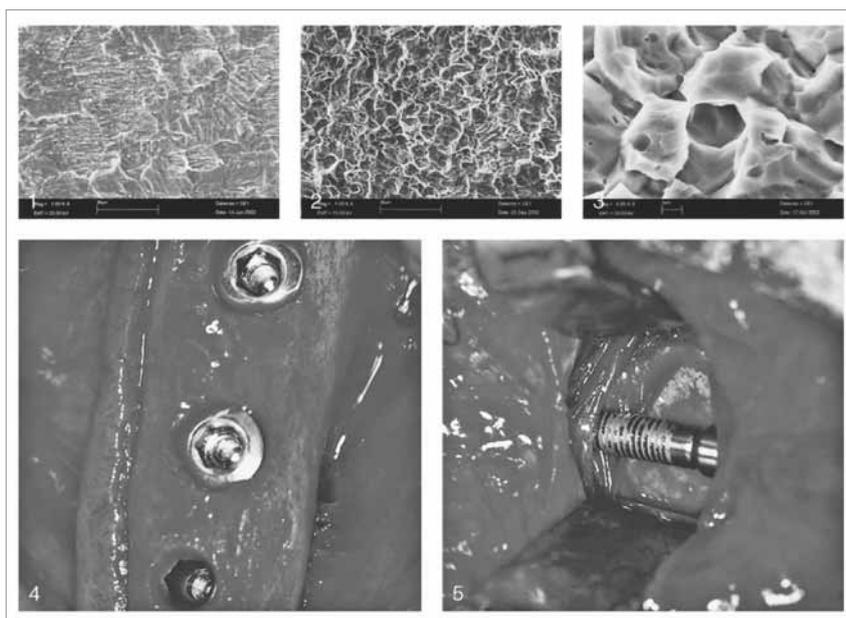


Fig. 1. Implant surface before acid-etched treatment. SEM X1000.

Fig. 2. Implant surface obtained after organic acid mixture treatment. SEM X1000.

Fig. 3. High magnification of the treated surface showing the microconcavities' appearance. SEM X5000.

Fig. 4. Clinical image showing implants inserted in the hemimandible of nonhuman primates.

Fig. 5. Clinical image showing a test implant inserted in the rectus abdominus muscle of nonhuman primates.

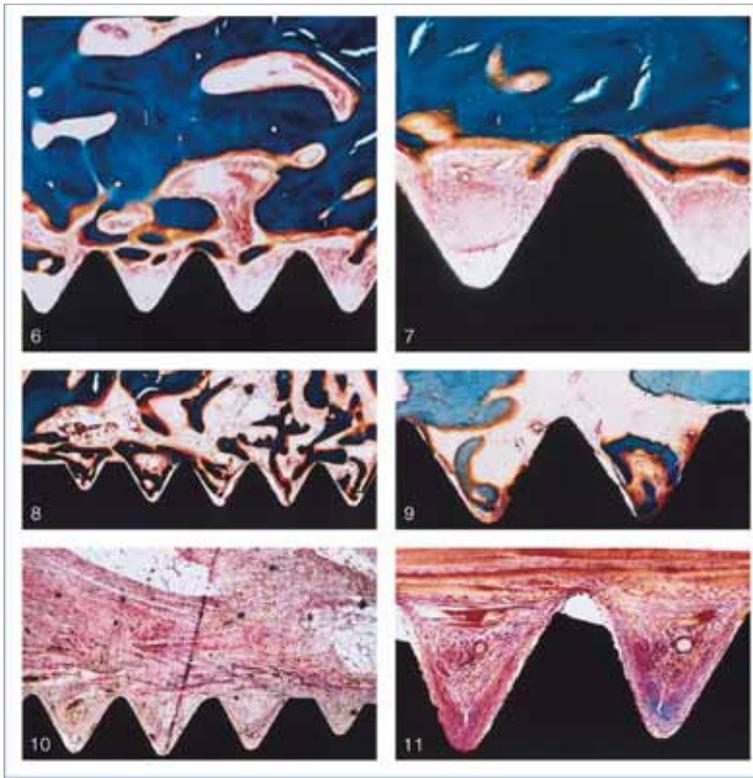


Fig. 6. Control (machined) implant. After a 1-month healing period, scarce bone formation, especially within the concavities, was detected. Goldner trichrome stain X10.

Fig. 7. Control (machined) implant. Higher magnification of the bone-implant interface. No bone formation within the concavities was detected. Goldner trichrome stain X30.

Fig. 8. Test (acid-etched) implant. After 1 month of healing, newly formed bone (both osteoid and mineralized) filled the spaces between the old bone and the implant surface. New bone formation directly on the implant surface and within the concavities was observed. Goldner trichrome stain X10.

Fig. 9. High magnification of the bone-implant interface. Newly formed bone was evident within the concavities along with the presence of newly formed vessels and osteoblast activity. Goldner trichrome stain X30.

Fig. 10. Control (machined) implants harvested from the extra skeletal site (muscle) after 1 month. Only a scarce amount of connective tissue was attached to the implant surface. Goldner trichrome stain X10.

Fig. 11. Test (acid-etched) implant. It was possible to observe the presence of new connective and vascular tissue. Goldner trichrome stain X30.

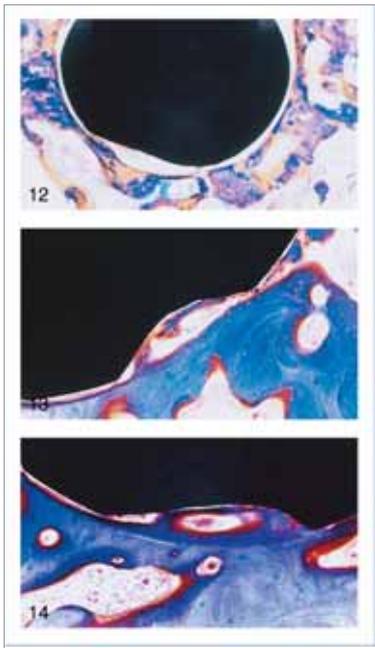


Fig. 12. Control (machined) implant harvested from human after 2 months. No bone formation on the implant surface was detected. Goldner trichrome stain X30.

Fig. 13. Test (acid-etched) implant. It was possible to observe newly formed bone directly on the implant surface and especially within the concavities. Goldner trichrome stain X30.

Fig. 14. Test (acid-etched) implants. Axial section showing new bone formation within the concavities. Osteoid matrix and newly formed small vessels were present. Goldner trichrome stain X20.

## Direct laser metal sintering as a new approach to fabrication of an isoelastic functionally graded material

Direct laser metal sintering as a new approach to fabrication of an isoelastic functionally graded material for manufacture of porous titanium dental implants

Traini T, Mangano C, Sammons RL, Mangano F, Macchi A, Piattelli A

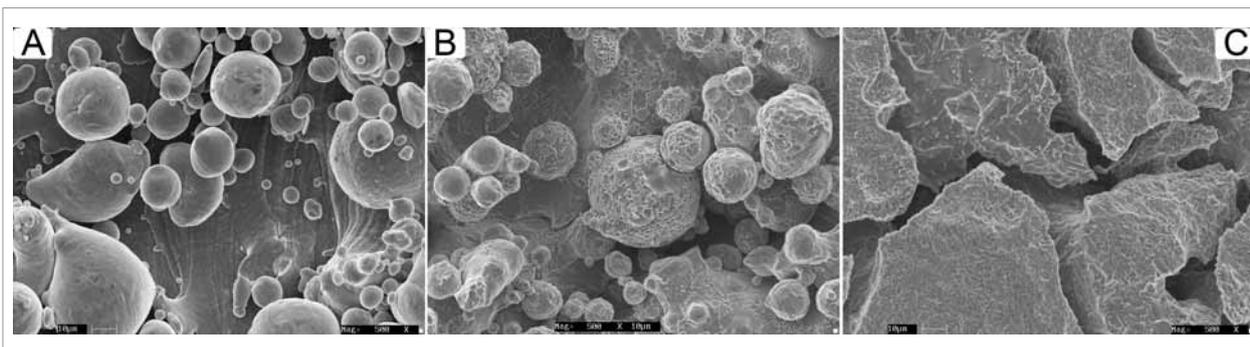
**Dental Materials**  
2008; 24:1525-1533

**Objectives:** This work focuses on a titanium alloy implants incorporating a gradient of porosity, from the inner core to the outer surface, obtained by laser sintering of metal powder. Surface appearance, microstructure, composition, mechanical properties and fractography were evaluated.

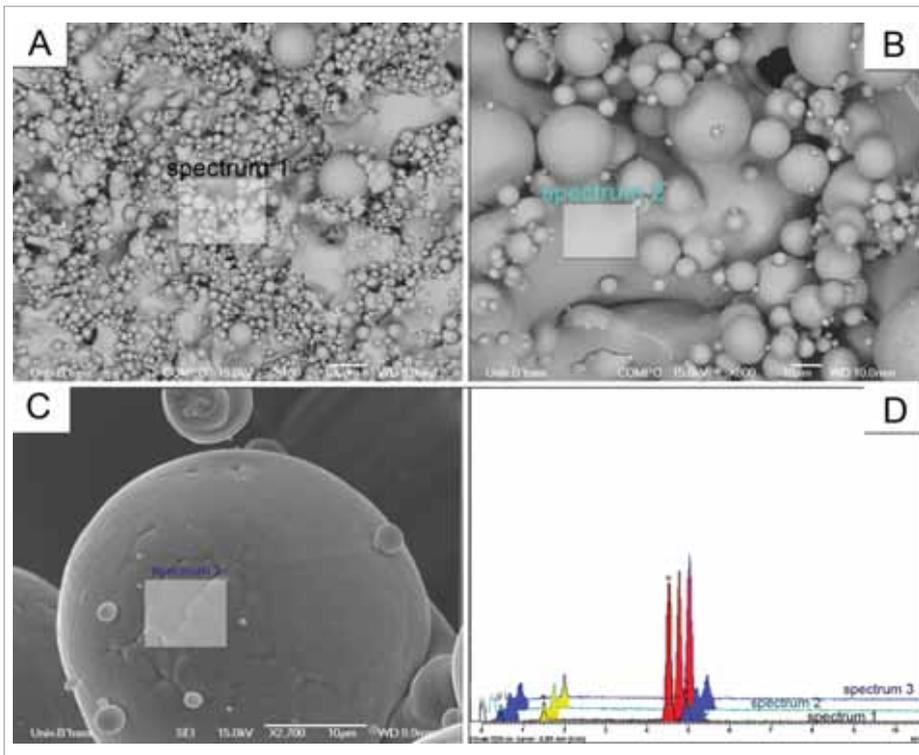
**Methods:** All the specimens were prepared by a selective laser sintering procedure using a Ti-6Al-4V alloy powder with a particle size of 1–10  $\mu\text{m}$ . The morphological and chemical analyses were performed by SEM and energy dispersive X-ray spectroscopy. The flexure strength was determined by a three-point bend test using a universal testing machine. The surface roughness was investigated using a confocal scanning laser microscope. The surface roughness variation was statistically evaluated by use of a Chi square test. A p value of  $<0.05$  was considered statistically significant.

**Results:** The original surface microstructure consisted of roughly spherical particles, diameter range 5–50  $\mu\text{m}$ . After exposure to hydrofluoric acid some of these were removed and the microsphere diameter then ranged from 5.1  $\mu\text{m}$  to 26.8  $\mu\text{m}$ . Following an organic acid treatment, particles were replaced by grooves 14.6–152.5  $\mu\text{m}$  in width and 21.4–102.4  $\mu\text{m}$  depth. The metal core consisted of columnar beta grains with alpha and beta laths within the grains. The alloy was composed of 90.08%Ti, 5.67%Al and 4.25%V. The Young's modulus of the inner core material was  $104 \pm 7.7$  GPa; while that of the outer porous material was  $77 \pm 3.5$  GPa. The fracture face showed a dimpled appearance typical of ductile fracture.

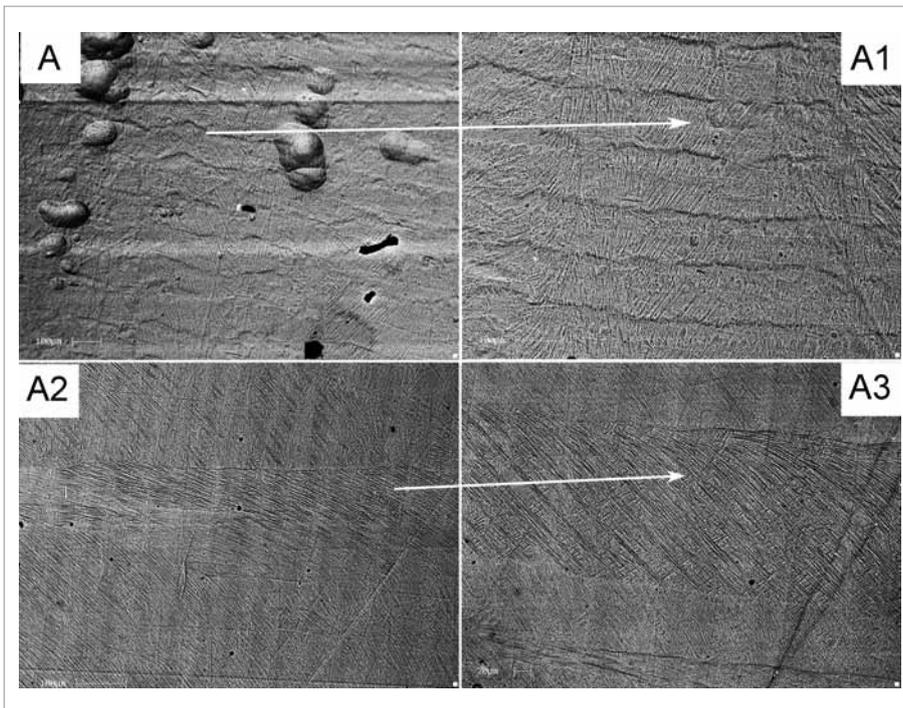
**Significance:** In conclusion, laser metal sintering proved to be an efficient means of construction of dental implants with a functionally graded material which is better adapted to the elastic properties of the bone. Such implants should minimize stress shielding effects and improve long-term performance.



SEM images at 500 $\times$  magnification of surface's DLMS fabricated discs after different treatments. (A) Untreated disc; (B) disc treated with hydrofluoric acid; (C) disc treated with organic acid.



SEM and EDS analysis of untreated specimens at different magnifications. (A) 100 $\times$ , size bar=100 $\mu$ m; (B) 300; size bar=10 $\mu$ m; (C) 2700 $\times$ , size bar=10 $\mu$ m. (D) EDS spectra obtained from the sites indicated in each image. The spectra from the different areas were identical. Red peaks, titanium; blue, vanadium; yellow, aluminum.



SEM-BSE images at 100 and 400 $\times$  magnification of DLMS specimen's microstructure in section. (A) is the microstructure in the porous region with some similar layer banding pattern overlapped, as is best visible in (A1) at 400 $\times$  magnification. (A2) is the microstructure of the core of the specimen with different overlapped layer banding as is best visible in (A3) at 400 $\times$  magnifications.

### The induction of bone formation by smart biphasic hydroxyapatite tricalcium phosphate biomimetic matrices

The induction of bone formation by smart biphasic hydroxyapatite tricalcium phosphate biomimetic matrices in the non-human primate *Papio ursinus*

Ripamonti U, Richter PW, Nilen RWN, Renton L

**Journal of Cellular and Molecular Medicine**  
2008; 12(6B):2609-2622

The spontaneous induction of bone formation in heterotopic rectus abdominis and orthotopic calvarial sites by coral-derived biomimetic matrices of different chemical compositions was investigated in a long-term study in the non-human primate *Papio ursinus*. Coral-derived calcium carbonate constructs were converted to hydroxyapatite by hydrothermal exchange. Limited conversion produced hydroxyapatite/calcium carbonate (HA/CC) constructs of 5% and 13% hydroxyapatite. Rods of 20 mm in length and 7 mm in diameter were implanted in heterotopic rectus abdominis sites: discs 25 mm in diameter were implanted in orthotopic calvarial defects of six adult non-human primates *P. ursinus*. Heterotopic samples also included fully converted hydroxyapatite replicas sintered at 1100°C. To further enhance spontaneous osteoinductive activity, fully converted hydroxyapatite replicas were coated with the synthetic peptide P15 known to increase the adhesion of fibroblasts to anorganic bovine mineral. Bone induction was assessed at 60, 90 and 365 days by histological examination, alkaline phosphatase and osteocalcin expression, as well as by expression of BMP-7, GDF-10 and collagen type mRNAs. Induction of bone occurred in the concavities of the matrices at all time points. At 365 days, bone marrow was evident in the P15-coated and uncoated implants. Resorption of partially converted calcium carbonate/hydroxyapatite was apparent, as well as remodeling of the newly formed bone. Northern blot analyses of samples from heterotopic specimens showed high levels of expression of BMP-7 and collagen type IV mRNA in all specimen types at 60 days, correlating with the induction of the osteoblastic phenotype in invading fibrovascular cells. Orthotopic specimens showed prominent bone formation across the different implant constructs. The concavities of the matrices biomimeticize the remodeling cycle of the osteonic primate cortico-cancellous bone and promote the ripple-like cascade of the induction of bone formation. This study demonstrates for the first time that partially converted HA/CC constructs also induce spontaneous differentiation of bone, albeit only seen one year post-implantation.

## Self-inducing shape memory geometric cues embedded within smart hydroxyapatite-based biomimetic matrices

Self-inducing shape memory geometric cues embedded within smart hydroxyapatite-based biomimetic matrices

Ripamonti U, Richter PW, Thomas ME

**Experimental**  
2007; 120(7):1796-1807

**Background:** The authors investigated in nonhumans primates (*Papio ursinus*) whether it is possible to engineer biomimetic matrices that induce the differentiation of osteoblastic cells expressing selected osteogenic mRNA species of the transforming growth factor (TGF)- $\beta$  superfamily.

**Methods:** Four types of sintered hydroxyapatite and biphasic hydroxyapatite/tricalcium phosphate bioceramics were evaluated as osteoinductive self-inducing biomimetic matrices. Matrices were fabricated with a series of repetitive concavities that initiate the induction of bone formation as a secondary response. Single-phase hydroxyapatite, biphasic hydroxyapatite/tricalcium phosphate, and carbon-impregnated single-phase hydroxyapatite, the latter with fine and coarse porosities, were implanted heterotopically in the rectus abdominis. Specimens for orthotopic calvarian implantation were a total of 16 macroporous disks 25 mm in diameter of single-phase hydroxyapatite and biphasic hydroxyapatite/tricalcium phosphate.

**Results:** Heterotopic specimens 90 and 180 days after implantation showed the induction of bone within concavities of the biomimetic matrices. Northern blot analyses of heterotopic specimens showed that carbon-impregnated single-phase hydroxyapatite specimens induced high expression of osteogenic protein-1 mRNA, correlating with the induction of bone formation. Collagen type IV mRNA was highly expressed, particularly on day 90, by all the implanted matrices. Orthotopic specimens showed substantial bone formation across the implanted constructs.

**Conclusions:** Self-induced bone has been achieved via the development of osteogenic molecular signal expressed by differentiating osteoblastic-like cells, later secreted and embedded into the smart concavities of the biomimetic matrices. The described biomimetic matrices induce de novo bone formation even in the absence of exogenously applied osteogenic proteins of the TGF- $\beta$  superfamily.

*Biological investigation of an experimental laser sintered titanium implant surface*

Mangano F, Sammons RL, Mangano C, Montini S, Piattelli A

*Clinical Oral Implant Research*  
2007; 18(5):333

**Biological investigation of an experimental laser sintered titanium implant surface**

**Introduction:** As implant surface micro-topography deeply affects bone healing, research topics like implant surfaces and the bone-implant interface have gained significant importance in modern implant dentistry. Recent works support the concept that surfaces characterized by specific geometric features like cavities, grooves and pores could stimulate new bone formation, even in extra-skeletal sites, through the fascinating mechanisms of osteoinduction 2-3-4. Rapid prototyping is a revolutionary technique which enables to directly generate physical objects with defined and desired structure and shape, on the basis of virtual 3D data. Direct laser metal forming (DLMF) is a rapid prototyping application in which the basic material particles are fused in a laser focus. The aim of this study was to evaluate biological behaviour of a brand new laser sintered titanium implant surface (Fig.1), rich in pores, cavities and grooves (Leader-Novaxa SRL, Milan, Italy), versus a conventional machined titanium surface.

**Materials and methods:** Ti powders with a particle size of 25-45 micron were used as basic material. These particles were fused in a laser focus, using a powerful Yb (Ytterbium) fibre laser system, with a capacity to build a volume up to 250mm x 250mm x 215mm, in a wavelength of 1060-1100nm, with a nominal power 200W (190W in the building area). 10 experimental, laser sintered titanium discs were manufactured. The original surface microstructure consisted of roughly spherical particles, diameter ranging from 5 to 50µm, some of which were remnants of the original powder. Exposure to organic acid mixture was subsequently performed, in order to remove non-adherent titanium particles, and the final test surface was obtained, in which particles were replaced by grooves ranging from 14.6 to 152.5 µm width and 21.4 to 102.4 µm depth. On the other hand, 10 conventional machined titanium discs were prepared as control surface. SEM evaluation of calvarian rat osteoblasts cultured on both test and control discs was finally performed, to assess "invitro" biological behaviour of different surfaces. Primary rat (3-dayold) calvarial osteoblasts were cultured for 10 days until confluent. Cells were harvested using trypsin and re-suspended in culture medium to a density of 5 x 10<sup>4</sup> cells/ml. Discs were subsequently placed in wells covered with cell suspension (1ml per disc). Cells were cultured on discs for 9 days, than fixed and processed for SEM evaluation.

**Results:** All test specimens showed a peculiar surface, with repeated cavities, carved by deep, narrow intercommunicating crevices, shallow depressions and deep, rounded pits of variable shape and size. The cavities extended beneath the surface to form a three-dimensional network of intercommunicating passages (Fig. 2) In this context, cells appeared sparse in cavities, climbing grooves, attached to protruding features of surface, tightly stretched overlying pits (Fig. 3-4). Cell shape was governed by attachment and surface features, with some clear evidence of extra-cellular matrix secretion (Fig. 5). In control specimens, on the other hand, surface was completely covered with confluent layer of cells. Cells flattened, closely adhering to surface, with no evidence of extra-cellular matrix deposition.

**Conclusions:** The test surface appears to be biocompatible and to stimulate cell attachment and cell growth in a manner which other studies have indicated should promote the expression of a mature osteoblastic phenotype, inducing bone formation. This study demonstrated the potential application of sintering process for titanium to obtain reproducible surface architecture for engineered implants, which can be additionally treated through acid etching procedure, in order to increase bone.



**Morphological investigation of an experimental laser sintered titanium implant**

*Morphological investigation of an experimental laser sintered titanium implant*

Raspanti M, Mangano C, Macchi A, Mangano F, Piattelli A, Traini T

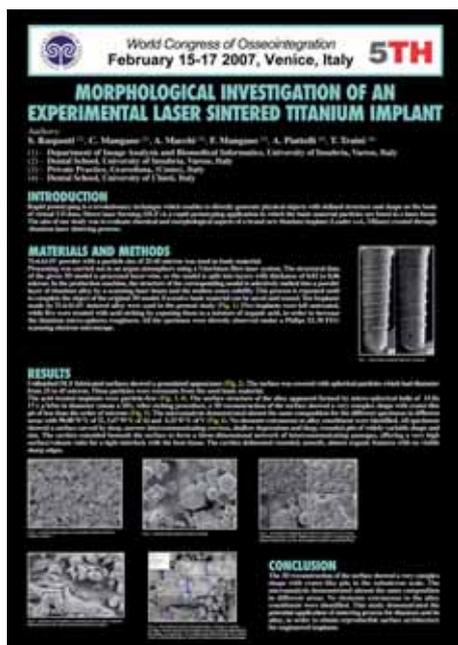
*European Journal of Implant Prosthodontics*  
2007; 1(3):28

**Introduction:** Rapid prototyping is a revolutionary technique which enables to directly generate physical objects with defined structure and shape on the basis of virtual 3D data. Direct laser forming (DLF) is a rapid prototyping application in which the basic material particles are fused in a laser focus. The aim of our study was to evaluate chemical and morphological aspects of a brand new titanium implant (Leader srl, Milano) created through titanium laser sintering process.

**Materials and methods:** Ti-6Al-4V powder with a particle size of 25-45 micron was used as basic material. Processing was carried out in an argon atmosphere using a Ytterbium fibre laser system. The structural data of the given 3D model is processed layer-wise, so the model is split into layers with thickness of 0.02 to 0.06 micron. In the production machine, the structure of the corresponding model is selectively melted into a powder layer of titanium alloy by a scanning laser beam and the molten zones solidify. This process is repeated until to complete the object of the original 3D model. Excessive basic material can be saved and reused. Ten implants made by Ti-6Al-4V sintered alloy were used in the present study. Five implants were left untreated, while five were treated with acid etching by exposing them to a mixture of organic acid, in order to increase the titanium micro-spheres roughness. All the specimen were directly observed under a Philips XL30 FEG scanning electron microscope.

**Results:** Unfinished DLF fabricated surfaces showed a granulated appearance. The surface was covered with spherical particles which had diameter from 25 to 45 micron. These particles were remnants from the used basic material. The acid treated implants were particle-free. The surface structure of the alloy appeared formed by micro-spherical balls of  $15.8 \pm 17.1 \mu\text{m}^5\text{m}$  in diameter (mean  $\pm$  SD). After etching procedure, a 3D reconstruction of the surface showed a very complex shape with crater-like pit of less than the order of microns. The microanalysis demonstrated almost the same composition for the different specimens in different areas with 90.08 W% of Ti, 5.67 W% of Al and 4.25 W% of V. No elements extraneous to alloy constituent were identified. All specimens showed a surface carved by deep, narrow intercommunicating crevices, shallow depressions and deep, rounded pits of widely variable shape and size. The cavities extended beneath the surface to form a three-dimensional network of intercommunicating passages, offering a very high surface/volume ratio for a tight interlock with the host tissue. The cavities delineated rounded, smooth, almost organic features with no visible sharp edges.

**Conclusion:** The 3D reconstruction of the surface showed a very complex shape with crater-like pits in the submicron scale. The microanalysis demonstrated almost the same composition in different areas. No elements extraneous to the alloy constituent were identified. This study demonstrated the potential application of sintering process for titanium and its alloy, in order to obtain reproducible surface architecture for engineered implants.



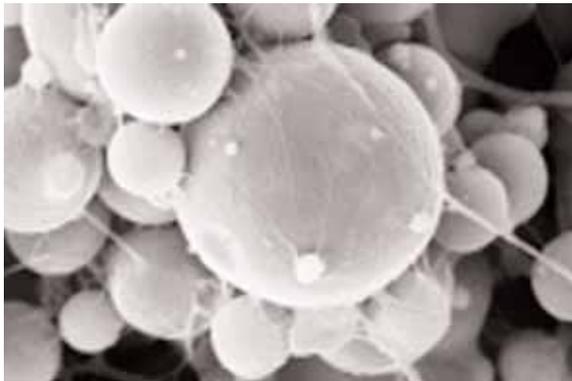
## Producing dental implants by Direct Laser Forming

Impianti dentali in titanio sinterizzato  
tramite laser

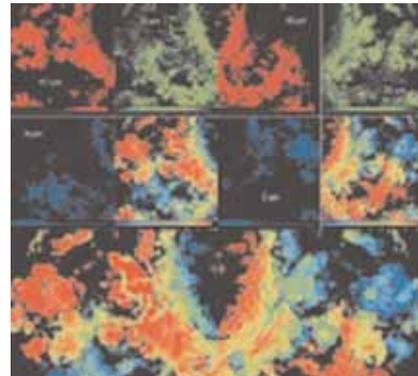
Mangano C, Traini T, Piattelli A,  
Macchi A, Mangano F,  
Montini S, Mangano A

**Italian Oral Surgery**  
2006; 4:7-12

Dental implants are mainly made by titanium of different grades, and sometimes in order to improve the mechanical proprieties of the appliances a Ti 6Al 4V alloy is used. The surface texture and composition of the implants is a factor that influences the osseointegration especially in the initial phases of osteogenesis. The aim of this study was to analyze the macroscopic structure and the chemical composition of a titanium dental implant obtained by a new sintering process. Ten specimens made by Ti6Al4V sintered alloy were used in the present study. Five specimens was exposed to a mixture of organic acid. The surface structure of the alloy appeared formed by microspherical balls. After the etching procedure a 3D reconstruction of the surface showed a very complex shape with crater-like pits in the submicrons scale. The microanalysis demonstrated almost the same composition in different areas. No elements extraneous to the alloy constituent were identified. This study demonstrated the potential application of sintering process for titanium and its alloy to obtain reproducible surface architecture for engineered implants. The new DLF (Direct Laser Forming) procedure permit to obtain from 3D models dental implants with complex surface geometries according to tissue engineering.



SEM image of the early stages of the fibrin coagulum formation on the titanium sintered surface



SEM image with confocal laser in which it is possible to see the fibrin coagulum all over the surface

## Implanto-prosthetic treatment by means of Leader system

Leczenie implanto-protetyczne z  
zastosowaniem wszczepów systemu  
Leader

Mierzwinska-Nastalska E, Feder T,  
Spiechowicz E

**Protet. Stomatol.**  
LVI, 5, 367-373, 2006

The removable implant-supported prosthesis is the treatment of choice in some clinical situations. A case report illustrating the prosthetic procedures of this treatment option, including laboratory fabrication, is presented. This report describes the new Leader dental implants and Sphero-Flex system. The future observation will demonstrate the advantages and disadvantages of this implants system.

### Bioengineering applied to osseointegrated implant dentistry: clinical reality or pure research?

La bioingegneria applicata all'implantologia osteointegrata: realtà clinica o ricerca pura?

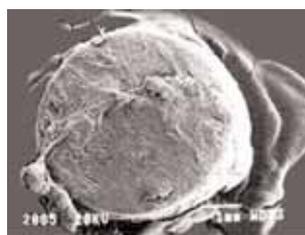
Mangano C, Ripamonti U, Piattelli A, Mangano F, Montini S

**Implantologia Orale**  
2006; 1:47-56

The study of bone healing at bone/implant interface has achieved great importance in modern oral implantology. By now, chemical composition and implant surface microstructure are well-know factors, capable of affecting osseointegration. After implant placement, early biological events are fundamental, and surfaces with peculiar geometric characteristics can effectively promote bone healing, interacting with specific molecules and proteins. Bioengineered implant surfaces can guide these biological events, to improve osseointegration both temporally (in order to accelerate bone healing process) and spatially (with the purpose to obtain complete bone/implant contact).



Titanium disc (test) from the muscle.



Titanium disc (control) from the muscle.

### A new modified titanium implant surface: histological evaluation in non human primates and humans

A new modified titanium implant surface: histological evaluation in non human primates and humans

Mangano C, Macchi A, Mangano A

**Dental Horizon**  
2006; 4(2):313-317

The purpose of this study was to provide histological evidence of the effect of a new acid-etching treatment on early bone formation.

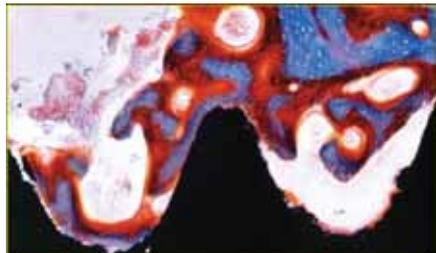
The histomorphometric evaluation demonstrated that the implant surface geometry can promote bone formation creating a special microenvironment where angiogenesis is the predominant aspect. The modification of the implant topography with a new acid treatment can optimize the interaction with host tissue obtaining bone formation in less amount of time. For the purpose of this study, 10 threaded microimplants (Ø 3,2 mm x 5 mm) and 24 standard implants (Ø 3,75 mm x 11,5 mm) of pure titanium (Leader s.r.l. Milano Italy) were used. Of the 10 microimplants, 5 had machined surfaces (control) and 5 were treated with an organic acid mixtrure (test) (Fig 1,2).Of the 24 standard implants 12 were prepared with machined surfaces (control) and 12 with organic acid mixture (test).

The modification of an implant surface topography can optimize the interaction with host tissue during healing wound to obtain the better healing in less time possible.

This study in the non human primate and in the human has demonstrated that a new titanium implant with an acid-treated surface (organic acids) has the capacity of inducing a larger and faster osteointegration if compared with the same implant with a machimed surface. Conclusion is that the surface configuration of an implant is a crucial factor for rapid and successfull osteointegration.



Magnification of bone implant interface. New bone was evident within concavity with angiogenesis and osteoblast activity.



Test implant with axial section show new bone formation within concavity. Florid osteoid and angiogenesis was evident.

### Three dimensional custom made porous hydroxyapatite for bone regeneration

Three dimensional custom made porous hydroxyapatite for bone regeneration

Mangano C, Macchi A, Mangano F, Montini S, Mangano A

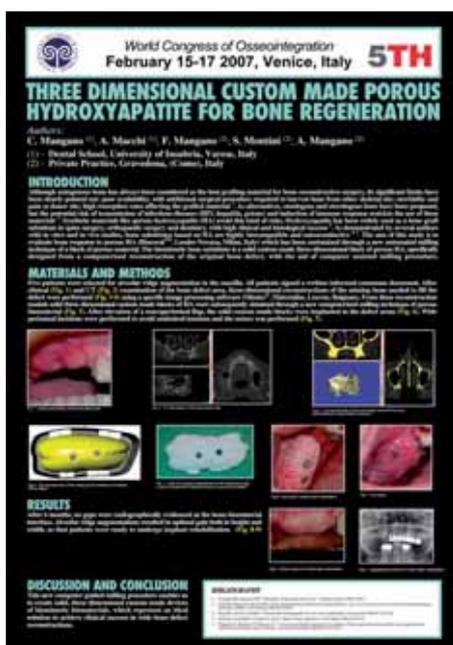
Clinical Oral Implant Research  
2006; 17(4):249

**Introduction:** Although autogenous bone has always been considered as the best grafting material for bone reconstructive surgery, its significant limits have been clearly pointed out: poor availability, with additional surgical procedure required to harvest bone from other skeletal site; morbidity and pain at donor site; high resorption rates affecting the grafted material. As alternatives, homologous and heterologous bone have been proposed, but the potential risk of transmission of infectious diseases (HIV, hepatitis, prions) and induction of immune response restricts the use of these materials. Synthetic materials like porous hydroxyapatite (HA) avoid this kind of risks. Hydroxyapatite has been widely used as a bone graft substitute in spine surgery, orthopaedic surgery and dentistry, with high clinical and histological success. As demonstrated by several authors with in vitro and in vivo studies, bone substitutes based on HA are highly biocompatible and osteoconductive. The aim of this study is to evaluate bone response to porous HA (Biocoral™ Leader-Novaxa, Milan, Italy) which has been customized through a new automated milling technique of a block of porous material. The biomimetic bone substitute is a solid custom made three-dimensional block of porous HA, specifically designed from a computerized reconstruction of the original bone defect, with the aid of computer assisted milling procedure.

**Materials and Methods:** Five patients were selected for alveolar ridge augmentation in the maxilla. All patients signed a written informed consensus document. After clinical and CT examination of the bone defect area, three-dimensional reconstructions of the missing bone needed to fill the defect were performed using specific image processing software (Mimics® Materialise, Leuven, Belgium). From these reconstruction models solid three dimensional custom made blocks of HA were subsequently obtained through a new computerized milling technique of porous periosteal incisions were performed to avoid undesired tensions and the suture was performed.

**Results:** After 6 months, no gaps were radiographically evidenced at the bone-biomaterial interface. Alveolar ridge augmentations resulted in optimal gain both in height and width, so that patients were ready to undergo implant rehabilitation.

**Discussion and Conclusion:** This new computer guided milling procedure enables us to create solid, three dimensional custom made devices of biomimetic biomaterials, which represent an ideal solution to achieve clinical success in wide bone defect reconstructions.



### ***Histologic evaluation of immediately loaded titanium implants retrieved from humans***

*Histologic evaluation of immediately loaded titanium implants retrieved from humans*

Mangano F, Mangano C, Piattelli A, Iezzi G, Perrotti V

*Clinical Oral Implant Research*  
2006; 17(4):158

**Introduction:** with the introduction of rough surfaced implants there is the possibility to increase bone to implant contact, allowing shortened healing times. The aim of this study was to document the early healing processes and bone response to a new implant surface geometry, characterized by a series of repeated concavities, in an immediate loading protocol in humans.

**Materials and methods:** This study was approved by the Ethics Committee of the University of Chieti-Pescara, Italy, and the patients signed a written informed consensus document. Ten dental implants 2.7 x 10 mm<sup>2</sup> (Leader S.r.l., Milano, Italy) were inserted in the interforaminal area of five edentulous patients, and then immediately loaded with temporary overdenture. After 1 month of function, all implants and surrounding tissues were retrieved with a 4 mm trephine drill, processed and examined with a transmitted light microscope and fluorescence microscope.

**Result:** Newly formed bone was observed on the implant surface with a bone-implant contact percentage of 56.3 ± 4.8. Active osteoblasts in the process of secreting osteoid matrix were observed on the surface of the implants. The new bone formation appeared to start consistently in the concavities on the implant surface, while a lesser amount of bone was found in the convexities.

**Discussion and conclusion:** immediate loading of implants is a predictable and well-documented procedure. This study shows that concavities on the implant surface, representing probably an ideal microenvironment for bone formation, are the first sites of bone formation and could promote a faster and greater bone apposition.

### ***Surface microstructure and fibrin extension on titanium laser sintered specimens***

*Surface microstructure and fibrin extension on titanium laser sintered specimens*

Iezzi G, Traini T, Mangano C, Piattelli A

*Journal of Clinical Periodontology*  
2006; 73-80

Rehabilitation of the edentulous posterior maxilla with dental implants is often very difficult because of insufficient bone volume produced by pneumatization of the maxillary sinus and by crestal bone resorption. The maxillary sinus augmentation can be an effective treatment option.

The purpose of this study was to show the histological behaviour of a biomimetic hydroxyapatite in the maxillary sinus augmentation in humans. Twelve patients were selected and after obtaining the informed consent, a total of 22 screw-type implants (Leader Italia, Milano, Italy) were placed simultaneously with sinus augmentation.

The x-ray examinations showed the presence of dense bone around and above the implants in the maxillary sinus.

### FESEM and microanalysis investigation of an experimental sintered titanium alloy implant

FESEM and microanalysis investigation of an experimental sintered titanium alloy implant

Iezzi G, Traini T, Mangano C, Sammons RL, Piattelli A

Academy of Osseointegration 21st Annual meeting, March 2006

**Introduction:** Dental implants are mainly made of titanium of different grades, and sometimes in order to improve the mechanical proprieties of the appliances a Ti 6Al 4V alloy is used. The surface texture and composition of the implants is a factor that influences the osseointegration especially in the initial phases of osteogenesis.

**Aim:** The aim of this study was to analyze the macroscopic structure and the chemical composition of an experimental titanium dental implant obtained by a new sintering process.

**Materials and Methods:** two specimens made by Ti6Al4V sintered alloy were used in the present study. The specimens were investigated in a Schottky Field Emission Gun Scanning Electron Microscope (JEOL JSM-7000F, JEOL Ltd, Tokyo, Japan) equipped with an Energy Dispersive Spectrometry analysis (EDS-INCA, Oxford Instruments, Oxon, UK). One specimen was exposed to a vapor of 40% hydrofluoric acid at room temperature for five minutes in order to increase the roughness of the titanium micro-spheres.

**Results:** The surface structure of the alloy appeared to be formed by micro-spheres of diameter  $15.8 \pm 7.1 \mu\text{m}$  (mean  $\pm$  SD), with a minimum of 5.1 and a maximum of 26.8. After the etching procedure a 3D reconstruction of the surface showed a very complex shape with crater-like pits in the sub-micron scale (mean  $\pm$  SD:  $0.9 \pm 0.7 \mu\text{m}$ , with a minimum of 0.1  $\mu\text{m}$  and a maximum of 3.0  $\mu\text{m}$ ). The microanalysis demonstrated almost the same composition in different areas with 90.08 W% of Ti, 5.67 W% of Al and 4.25 W% of V. No elements extraneous to alloy constituent were identified.

**Conclusion:** This study demonstrated that the sintering process for Ti6Al4V alloy does not introduce differences in the elemental composition of the alloy at surface level. Moreover, the etching procedure produces an increase or the surface roughness in the sub-micron scale.

21st Annual Meeting Academy of Osseointegration  
March 16-18, 2006 Seattle, Washington

### FESEM and Microanalysis investigation of an experimental sintered titanium alloy implant

*Giovanna Iezzi<sup>\*</sup>, Tommaso Traini<sup>\*\*</sup>, Carlo Mangano<sup>\*\*</sup>, Rachel Sammons<sup>\*\*\*</sup> and Adriano Piattelli<sup>\*</sup>*  
*(<sup>\*</sup>Dental School, University of Chieti-Pescara, Italy; <sup>\*\*</sup>Private Practice, Gravescena CO, Italy; <sup>\*\*\*</sup>Dental School, University of Birmingham, UK)*  
*Dental School - University "G. D'Annunzio" of Chieti-Pescara ITALY*

**Abstract**  
Dental implants are mainly made of titanium of different grades, and sometimes in order to improve the mechanical proprieties of the appliances a Ti 6Al 4V alloy is used. The surface texture and composition of the implants is a factor that influences the osseointegration especially in the initial phases of osteogenesis. The aim of this study was to analyze the macroscopic structure and the chemical composition of an experimental titanium dental implant obtained by a new sintering process. Materials and Methods: two specimens made by Ti6Al4V sintered alloy were used in the present study. The specimens were investigated in a Schottky Field Emission Gun Scanning Electron Microscope (JEOL JSM-7000F, JEOL Ltd, Tokyo, Japan) equipped with an Energy Dispersive Spectrometry analysis (EDS-INCA, Oxford Instruments, Oxon, UK). One specimen was exposed to a vapor of 40% hydrofluoric acid at room temperature for five minutes in order to increase the roughness of the titanium micro-spheres. Results: The surface structure of the alloy appeared to be formed by micro-spheres of diameter  $15.8 \pm 7.1 \mu\text{m}$  (mean  $\pm$  SD), with a minimum of 5.1 and a maximum of 26.8. After the etching procedure a 3D reconstruction of the surface showed a very complex shape with crater-like pits in the sub-micron scale (mean  $\pm$  SD:  $0.9 \pm 0.7 \mu\text{m}$ , with a minimum of 0.1  $\mu\text{m}$  and a maximum of 3.0  $\mu\text{m}$ ). The microanalysis demonstrated almost the same composition in different areas with 90.08 W% of Ti, 5.67 W% of Al and 4.25 W% of V. No elements extraneous to alloy constituent were identified. Conclusion: This study demonstrated that the sintering process for Ti6Al4V alloy does not introduce differences in the elemental composition of the alloy at surface level. Moreover, the etching procedure produces an increase of the surface roughness in the sub-micron scale.

**KEYWORDS AND NOTATION**  
Ti-6Al-4V particles with a particle size of 25-30 microns were used as base material. Sintering was carried out in an argon atmosphere using a field emission gun. The surface texture and composition of the implants is a factor that influences the osseointegration especially in the initial phases of osteogenesis. The aim of this study was to analyze the macroscopic structure and the chemical composition of an experimental titanium dental implant obtained by a new sintering process. Materials and Methods: two specimens made by Ti6Al4V sintered alloy were used in the present study. The specimens were investigated in a Schottky Field Emission Gun Scanning Electron Microscope (JEOL JSM-7000F, JEOL Ltd, Tokyo, Japan) equipped with an Energy Dispersive Spectrometry analysis (EDS-INCA, Oxford Instruments, Oxon, UK). One specimen was exposed to a vapor of 40% hydrofluoric acid at room temperature for five minutes in order to increase the roughness of the titanium micro-spheres.

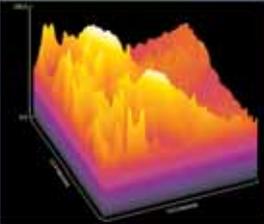


Fig. 1 - 3D reconstruction of the sintered titanium alloy implant after etching procedure.

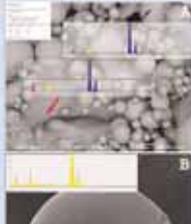


Fig. 2 - Aspect of the sintered titanium alloy implant surface.



Fig. 3 - Aspect of the sintered titanium alloy implant surface.

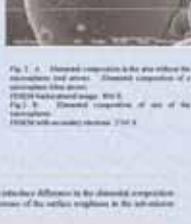


Fig. 4 - Aspect of the sintered titanium alloy implant surface.

### Implant prosthetic rehabilitation of elements with serious defect of bone tissue

Riabilitazione implantoprotesica di siti edentuli con gravi deficit ossei.  
Casi clinici

Silvetti M, Gualerni Tognola P

**Protech**  
2005; 4:29-37

In this study, the Authors describe two similar cases which were solved with the same surgical and implant restoration treatment, consequence of a evaluation which considers the Evidence Based dentistry, the professional experience, the teamwork and the patient's state of necessity.

Both adult patients had endosseous pathology deriving from chronic infectious process in the 4° quadrant. This pathology was solved with the extraction of the elements involved.

To the removal of cysts and granuloma cystic, there had a serious defect of bone tissue, which is treated with GBR and heterologous filler.

Then an implant-prosthetic rehabilitation (Leader Italia implants, Milano, Italy) and restoration of the occluded function followed.

The controls at a distance show a good aesthetic and functionality.

### Biomimetic surfaces and osteointegration: a study in non-human primates

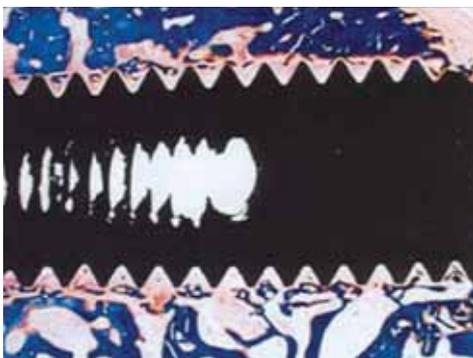
Superfici biomimetiche e osteointegrazione: studio su primati non umani

Mangano C, Ripamonti U, Montini S, Mangano F

**Italian Oral Surgery**  
2005; 2:9-17

Chemical and physical properties of implant surface play a fundamental role in bone formation. Surface roughness showed to have a great influence on the mechanisms of cellular differentiation, migration, proliferation and adhesion. The Authors have studied the biological behaviour of a new implant surface (Leader Italia, Milano, Italy) and its influence on bone synthesis in non-human primates (*Papio ursinus*).

Modified surface implants (test) and smooth-surface implants (control) were inserted in baboon's mandible and rectus abdomen muscle. After one month, the implants were removed and processed for histological analysis. Results indicated that new surface compared to control one produces a faster healing, offering a greater interface and a better bone density around implants.



Control (machined) implant harvested after 1 month healing. Scarce bone formation starting from old wall bone was evident, no bone formation within concavity is detected.



Test (acid-etched) implant harvested after 1 month of healing. new formed bone (both osteoid and mineralized) fills space between old bone and implant. New bone growth directly on implant surface and within concavity was evident.

*Histologic evaluation of bone response to a new geometric surface configuration in non-human primates*

Mangano C, Mangano F, Montini S

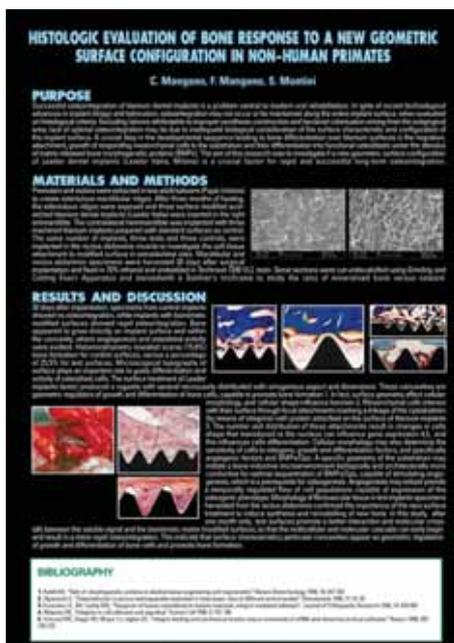
4<sup>th</sup> World Congress of  
Osseointegration, 2004  
In: Clinical Oral Implant Research

**Histologic evaluation of bone response to a new geometric surface configuration in non-human primates**

**Purpose:** Successful osteointegration of titanium dental implants is a problem central to modern oral rehabilitation. In spite of recent technological advances in implant design and fabrication, osteointegration may not occur or be maintained along the entire implant surface, when evaluated on histological criteria. Excluding failures attributable to improper prosthesis construction and bacterial colonization arising from the subgingival area, lack of optimal osteointegration may be due to inadequate biological consideration of the surface characteristic and configuration of the implant surface. A crucial step in the developmental sequence leading to bone differentiation over titanium surfaces is the migration, attachment, growth of responding mesenchymal cells to the substratum and their differentiation into functional osteoblasts under the stimulus of matrix released bone morphogenetic proteins (BMPs). The aim of this research was to investigate if a new geometric surface configuration of Leader dental implants (Leader Italia, Milano) is a crucial factor for rapid and successful long-term osteointegration.

**Materials and Methods:** Premolars and molars were extracted in two adult baboons (*Papio Ursinus*) to create edentulous mandibular ridges. After three months of healing, the edentulous ridges were exposed and three surface modified acid-etched titanium dental implants (Leader Italia) were inserted in the right hemimandibule. The contralateral hemimandibule was implanted with three machined titanium implants prepared with standard surfaces as control. The same number of implants, three tests and three controls, were implanted in the rectus abdominis muscle to investigate the soft tissue attachment to modified surface in extraskeletal sites. Mandibular and rectus abdominis specimens were harvested 30 days after surgical implantation and fixed in 70% ethanol and embedded in Technovit 7200 VLC resin. Serial sections were cut undecalcified using Grinding and Cutting Exact Apparatus and stained with a Goldner's trichrome to study the ratio of mineralized bone versus osteoid.

**Results and Discussion:** 30 days after implantation, specimens from control implants showed no osteointegration, while implants with biomimetic modified surfaces showed rapid osteointegration. Bone appeared to grow directly on implant surface and within the concavity, where angiogenesis and osteoblast activity were evident. Histomorphometry revealed scarce (15.8%) bone formation for control surfaces, versus a percentage of 25.5% for test surfaces. Microscopical topography of surface plays an important role to guide differentiation and activity of osteoblast cells. The surface treatment of Leader implants (tests) produced a rugosity with several microcavities distributed with omogeneous aspect and dimensions. These concavities are geometric regulators of growth and differentiation of bone cells, capable to promote bone formation. In fact, surface geometry affects cellular morphology, and cellular shape influences function. Mesenchymal cells interact with their surface through focal attachments involving a linkage of the cytoskeleton (by means of integrins) with protein absorbed on the surface of titanium implants. The number and distribution of these attachments result in changes in cells shape that transduced to the nucleus can influence gene expression and this influences cells differentiation. Cellular morphology may also determine the sensitivity of cells to mitogens, growth and differentiation factors, and specifically angiogenic factors and BMPs/Ops. A specific geometry of the substratum may initiate a bone-inductive microenvironment biologically and architecturally more conducive for optimal sequestration of BMPs/Ops, capable of stimulating angiogenesis, which is a prerequisite for osteogenesis. Angiogenesis may indeed provide a temporally regulated flow of cell populations capable of expression of the osteogenic phenotype. Morphology of fibrovascular tissue in test implants specimens harvested from the rectus abdominis confirmed the importance of the new surface treatment to induce synthesis and remodeling of new bone. In this study, after one month only, test surfaces promote a better interaction and molecular crosstalk between the soluble signal and the biomimetic matrix (modified surface), so that the multicellular and molecular cascade can early begin and result in a more rapid osteointegration. This indicates that surface characteristics particular concavities appear as geometric regulators of growth and differentiation of bone cells and promote bone formation.



## Implant geometric surface and osteogenesis. An histological study

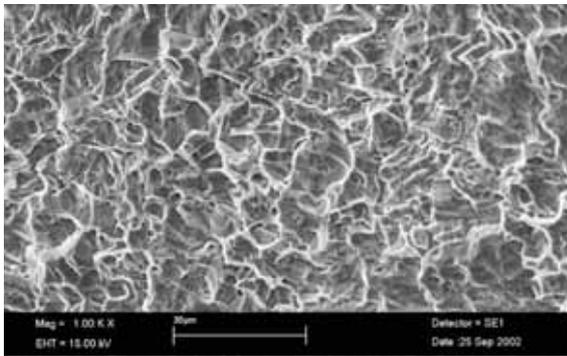
Geometria di superficie dell'impianto e osteogenesi: studio istologico

Mangano C, Bartolucci E, Ripamonti U

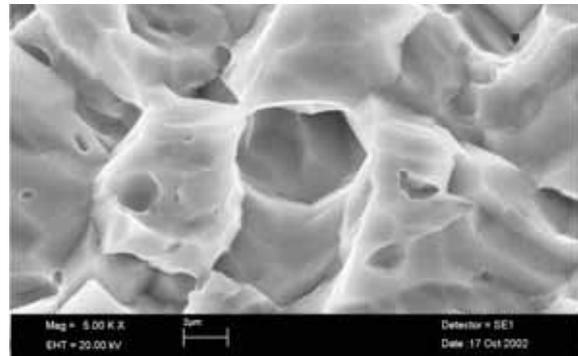
**Dental Cadmos**  
2003; 3:59-65

The aim of this study was to test the biological activity of a new titanium surface according to the principles of geometric induction in osteogenesis.

After obtaining a written consent, 8 mini titanium implant (Leader Italia, Milano, Italy) were implanted together with standard size implants in four patients. Tissue samples were taken after 3 and 4 months and prepared for light microscopy. Histological analysis has shown new bone formation in the concavities of test implants; while no bone formation could be observed in smooth control implants. The results suggest that this new implant surface may have an osteoinductive role according to the bone geometric induction principles.



Effect of the surface treatment carried out with a mixture of organic acids at low concentration



Distribution of shape of micro-cavities at a greater magnification (3000 x)





Literature review 2011 - 1st edition  
©2011 LEADER ITALIA srl

L | E | A | D | E | R  
I | T | A | L | I | A

LEADER ITALIA S.r.l.  
Via Aquileja, 49 - 20092 Cinisello Balsamo (MI) ITALY  
Tel. 02 61 86 51 - Fax 02 61 81 397  
e-mail: [info@leaderitalia.it](mailto:info@leaderitalia.it) - [www.leaderitalia.it](http://www.leaderitalia.it)

**INTERNATIONAL**  
Tel. +39 02 61 86 51 - Fax +39 02 61 29 06 76  
e-mail: [export@leaderitalia.it](mailto:export@leaderitalia.it) - [www.leaderitalia.it](http://www.leaderitalia.it)